09/700,165

L Number	Hits	Search Text	DB	Time stamp
1	29	bombesin same (sexual or impoten$5 or dysfunct$7 or erecti$5 or vagina$4 or peni$4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/26 20:41
2	486	bombesin and (sexual or impoten$5 or dysfunct$7 or erecti$5 or vagina$4 or peni$4)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/26 20:47
3	457	(bombesin and (sexual or impoten$5 or dysfunct$7 or erecti$5 or vagina$4 or peni$4)) not (bombesin same (sexual or impoten$5 or dysfunct$7 or erecti$5 or vagina$4 or peni$4))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/26 20:42
4	32	bombesin and sexual$3 same (impoten$5 or dysfunct$7 or erecti$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/26 20:48

```
=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
       BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
       CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU,
       DGENE, DRUGB, DRUGMONOG2, ...' ENTERED AT 21:33:46 ON 26 FEB 2004

68 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (bombesin? or neuromedin? or gastrin(2a)releas?(2a)peptide or GRP)
        120   FILE ADISCTI
         27   FILE ADISINSIGHT
          7   FILE ADISNEWS
        150   FILE AGRICOLA
         24   FILE ANABSTR
        193   FILE AQUASCI
         87   FILE BIOBUSINESS
         27   FILE BIOCOMMERCE
       7640   FILE BIOSIS
        111   FILE BIOTECHABS
        111   FILE BIOTECHDS
       1761   FILE BIOTECHNO
        562   FILE CABA
       1384   FILE CANCERLIT
       6224   FILE CAPLUS
        184   FILE CEABA-VTB
          2   FILE CEN
        123   FILE CIN
        198   FILE CONFSCI
          8   FILE CROPU
        242   FILE DISSABS
        417   FILE DDFB
       1508   FILE DDFU
  24 FILES SEARCHED...
       2592   FILE DGENE
        417   FILE DRUGB
         21   FILE DRUGMONOG2
         14   FILE IMSDRUGNEWS
       1695   FILE DRUGU
         12   FILE IMSRESEARCH
         26   FILE EMBAL
       5848   FILE EMBASE
       1504   FILE ESBIOBASE
        170   FILE FEDRIP
         42   FILE FROSTI
         23   FILE FSTA
        556   FILE GENBANK
         28   FILE HEALSAFE
        367   FILE IFIPAT
          3   FILE IMSPRODUCT
        619   FILE JICST-EPLUS
```

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          4   FILE KOSMET
       1584   FILE LIFESCI
          2   FILE MEDICONF
       5319   FILE MEDLINE
  47 FILES SEARCHED...
         22   FILE NIOSHTIC
        217   FILE NTIS
        148   FILE OCEAN
       3738   FILE PASCAL
         21   FILE PHAR
          2   FILE PHARMAML
          3   FILE PHIC
         41   FILE PHIN
       6412   FILE PROMT
          8   FILE RDISCLOSURE
       6464   FILE SCISEARCH
          2   FILE SYNTHLINE
       2248   FILE TOXCENTER
       3285   FILE USPATFULL
        137   FILE USPAT2
          1   FILE VETB
         15   FILE VETU
       3490   FILE WPIDS
  67 FILES SEARCHED...
       3490   FILE WPINDEX

  63 FILES HAVE ONE OR MORE ANSWERS,   68 FILES SEARCHED IN STNINDEX

L1   QUE (BOMBESIN? OR NEUROMEDIN? OR GASTRIN(2A) RELEAS?(2A) PEPTIDE OR GRP)
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            3490   FILE WPINDEX
L1              QUE (BOMBESIN? OR NEUROMEDIN? OR GASTRIN(2A) RELEAS?(2A) PEPTID
                ---------

     FILE 'BIOBUSINESS, BIOSIS, BIOTECHNO, CAPLUS, DGENE, DRUGU, EMBASE,
     ESBIOBASE, IFIPAT, LIFESCI, MEDLINE, PASCAL, PROMT, WPIDS, SCISEARCH,
     TOXCENTER' ENTERED AT 21:42:39 ON 26 FEB 2004
L2         56973 S L1
L3            18 S L2 AND (LIBIDO? OR ANORGASM? OR VAGINISMU? OR DYSPAREUNI? OR
L4            15 DUP REM L3 (3 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 21:47:11 ON 26 FEB 2004

     FILE 'BIOBUSINESS, BIOSIS, BIOTECHNO, CAPLUS, DGENE, DRUGU, EMBASE,
     ESBIOBASE, IFIPAT, LIFESCI, MEDLINE, PASCAL, PROMT, WPIDS, SCISEARCH,
     TOXCENTER' ENTERED AT 21:50:01 ON 26 FEB 2004
L5            43 S L2 AND (SEXUAL? OR ERECTIL?)(P)DYSFUNCT?

=> s l5 not l4
L6            32 L5 NOT L4

=> dup rem l6
DUPLICATE IS NOT AVAILABLE IN 'DGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L6
L7            25 DUP REM L6 (7 DUPLICATES REMOVED)

=> d l7 abs ibib kwic 1-25

L7   ANSWER 1 OF 25  PROMT  COPYRIGHT 2004 Gale Group on STN

AB     Following is a summary of news releases transmitted between 10 a.m. and
       noon by PR Newswire.  The full text of these releases is available at the
       PR Newswire for Journalists, http://media.prnewswire.com/.
        THIS IS THE FULL TEXT: COPYRIGHT 2003 PR Newswire Association, Inc.
ACCESSION NUMBER:    2003:572609  PROMT
TITLE:               PR Newswire National Summary, Monday, Nov. 3, Midnight to
                     10 a.m. ET.
SOURCE:              PR Newswire, (3 Nov 2003) .
PUBLISHER:           PR Newswire Association, Inc.
DOCUMENT TYPE:       Newsletter
LANGUAGE:            English
WORD COUNT:          8659
                     *FULL TEXT IS AVAILABLE IN THE ALL FORMAT*
TX     NEM001 11/03/2003 08:05 r f bc-MA-Dec-Res-Report
       (WALTHAM) Female Sexual Dysfunction Drug Market to
       Grow 10% From 2002 to
       2007
       PHM005 11/03/2003 08:43 r f bc-PA-Donegal-Grp-offer
       (MARIETTA) Donegal Group Inc. Announces Offering of Class A Common Stock

L7   ANSWER 2 OF 25  PROMT  COPYRIGHT 2004 Gale Group on STN

AB     Following is a summary of news releases transmitted between midnight and
       10 a.m. by PR Newswire.  The full text of these releases is available at
       the PR Newswire for Journalists, http://media.prnewswire.com/.
        THIS IS THE FULL TEXT: COPYRIGHT 2003 PR Newswire Association, Inc.
```

ACCESSION NUMBER: 2003:574497 PROMT
TITLE: PR Newswire National Summary, Tuesday, Nov. 4, Midnight to 10 a.m. ET.
SOURCE: PR Newswire, (4 Nov 2003) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 9163
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX PHTU005 11/04/2003 07:50 r f bc-AZ-Int-Insurance-**Grp**
(FLAGSTAFF) Mexican Insurance Leader Launches Two New Products
NYTU084 11/04/2003 09:31 r f bc-CT-CTT-Sunless-Tan
(FAIRFIELD) Competitive Technologies Licensees Show Progress On Sunless Tanning and **Sexual Dysfunction** Technologies

L7 ANSWER 3 OF 25 PROMT COPYRIGHT 2004 Gale Group on STN

AB Following is a summary of news releases transmitted between midnight and 10 a.m. by PR Newswire. The full text of these releases is available at the PR Newswire for Journalists, http://media.prnewswire.com/.
THIS IS THE FULL TEXT: COPYRIGHT 2003 PR Newswire Association, Inc.

ACCESSION NUMBER: 2003:511972 PROMT
TITLE: PR Newswire National Summary, Monday, Sept. 22, midnight to 10 a.m. ET.
SOURCE: PR Newswire, (22 Sep 2003) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 9277
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX NYM043 09/22/2003 08:07 r f bc-NJ-UMDNJ-men's-health
(PISCATAWAY) At UMDNJ-Robert Wood Johnson Medical School Survey Confirms Link Between Urinary Symptoms and **Sexual Dysfunction** in Men
PHM004 09/22/2003 09:03 r f bc-NY-Int-Biometric-**Grp**
(NEW YORK) International Biometric Group Announces Round Six of Comparative Biometric Testing

L7 ANSWER 4 OF 25 PROMT COPYRIGHT 2004 Gale Group on STN

AB Following is a summary of news releases transmitted this afternoon by PR Newswire. The full text of these releases is available at the PR Newswire for Journalists, http://media.prnewswire.com/.
THIS IS THE FULL TEXT: COPYRIGHT 2003 PR Newswire Association, Inc.

ACCESSION NUMBER: 2003:635423 PROMT
TITLE: PR Newswire National Summary, Wednesday, Dec. 17, 2003, Noon to 2 p.m. EST.
SOURCE: PR Newswire, (17 Dec 2003) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1918
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX PHW020 12/17/2003 12:28 r f bc-MD-Kingson-**Grp**-Sarbox
(BALTIMORE) The Kingson Group Limited and SAFE Risk Management Systems, LLC Introduce Sarbox ERIC(TM)
NEW021 12/17/2003 13:28 r f bc-MA-Two-New-**Erectile**

(BOSTON) Two New **Erectile Dysfunction** Drugs: How They Measure Up Against Viagra

L7 ANSWER 5 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 1
AN 2003-903554 [82] WPIDS
AB WO2003092670 A UPAB: 20031223

NOVELTY - Amino methyl ketone derivatives (I) and their salts, prodrugs or solvates are new.

DETAILED DESCRIPTION - Amino methyl ketone derivatives of formula (I) and their salts, prodrugs or solvates are new.

R1 = aromatic heterocycle CO2R5, CONR5R6, NR5R7, OR5, 1-6C(cyclo)alkyl, -C(O)N-morpholine, aryl (optionally 1-3 of NR5R5, N(R5)C(O)R5, NO2, halo, OR5 or R4NR5R5) or aromatic heterocycle (optionally substituted by 1-3 of halo, R5 or OR5);

Y = NR3 or CHR3;

R = 3-7C cycloalkyl, aromatic heterocycle optionally fused with a phenyl group, aryl (optionally fused with a heterocycle or a 3-7C cycloalkyl optionally containing (CO)), Oaryl, 1-6C alkyl (all optionally 1-3 R5, 1-6C alkenyl, aryl, OR4, OR5, OH, CF3, halo, SO2R5, NO2, SR5, CN, OCF3, CO2R5, C(O)R5, Oaryl, OR4aryl, R4OR5, C(NH)NR5R5, OC(O)1-6C alkyl and NR5R7), adamantyl or 1-6C alkenyl (optionally 1-2 phenyl).

R3 = 1-6C alkyl, 1-6C alkenyl, 1-6C alkynyl, aromatic heterocycle optionally fused with phenyl, phenyl optionally fused with phenyl, heterocycle or aromatic heterocycle, (all optionally substituted with 1-3 halo, CN, SR5, aromatic (heterocycle), R5, OR7, C(O)NR5R7, SO2NR5R7, NHSO2R5, OH, CF3, OR5, OR5, OR5OR5, NR5R7, CO2H, CO2R5, OC(O)R5, 3-7C cycloalkyl (optionally 1-6C alkyl, CH2OC(O)CH3 or phenyl optionally fused with a heterocycle, aromatic heterocycle optionally substituted with 1-3 groups of phenyl, R4, CN, OH, OR4Ph, OR4CO2R5, 1-6C alkynyl, R4OC(O)R5, R4SR5, OC(O)R5, CF3, OR7, OR4OR5, CO2R5, OR4, CO2R5, HNC(O)R5, 1-6C alkenyl, OCF3, NO2, halo, HNSO2R5, SO2NR5, C(O)NR5R5, C(NH)NR5R5, OR5, OC(O)R4-heterocycle, NR5R7, SR5 or tetrazole;

R4 = 1-6C alkyl;

R5 = H or 1-6C alkyl (optionally substituted with 1-3 of halo or OH);

R6 = H, heterocycle, 1-6C Oalkyl or 1-6C alkyl (optionally substituted with 1-3 of halo or OH) or NR56 to form 5-7 ring (optionally containing a further hetero moiety of O, NH, or S);

m, n, p and q = 0-2;

r = 0-4;

R7 = H or 1-6C alkyl (optionally substituted by an aryl group); and

R8, R9 = H or 1-6C alkyl or form a 3-7C cycloalkyl (optionally containing NR4, NH, O or S).

Provided that R1 = aryl or aromatic heterocycle group, R2 = phenyl, pyridyl or pyrimidinyl group (optionally substituted R8 and R9 combine to form a 3-7 cycloalkyl group), Y = NR3 and m, p, q and r = 0; the R3 cannot be 4-6C alkyl or 1C alkyl substituted by phenyl (optionally substituted by 1-3 groups of halo, O1-6C alkyl and NR5R7).

ACTIVITY - Tranquilizer; Antidepressant; Neuroleptic; Hypnotic; Nootropic; Respiratory-Gen; Hypotensive; Cytostatic; Gastrointestinal-Gen; Analgesic; Antiemetic; Anabolic; Eating - Disorders-Gen.; Endocrine-Gen; Vasotropic.

Tests described but no biological data given.

MECHANISM OF ACTION - **Bombesin** antagonist.

USE - (I) is useful for the treatment of anxiety, panic attacks, social phobia, depression, psychoses, sleeping disorders, memory

impairment, pulmonary hypertension, lung repair, lung development disorders, cancer treatment, prostate cancer, pancreatic cancer, hepatic porphyria, gastrointestinal secretory disturbances, gastrointestinal disorders, emesis, anorexia, pain, seasonal affective disorders (SAD), feeding disorders and **sexual dysfunction** (male **sexual dysfunction**, male **erectile dysfunction** and female **sexual dysfunction**) (claimed).

ADVANTAGE - (I) have utility in a variety of therapeutic areas, particularly female **sexual dysfunction** (FSD) especially in the FSD in female **sexual** arousal disorder (FSAD) and male **erectile dysfunction** (MED).

Dwg.0/0

ACCESSION NUMBER: 2003-903554 [82] WPIDS
DOC. NO. CPI: C2003-256997
TITLE: New amino methyl ketone derivatives are **bombesin** antagonists useful for the treatment of e.g. anxiety, hepatic porphyria and anorexia.
DERWENT CLASS: B05
INVENTOR(S): HIGGINBOTTOM, M; KESTEN, S R; LEWTHWAITE, R A; PRITCHARD, M C; RAWSON, D J; SCHELKUN, R M; YUEN, P
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO LLC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003092670	A1	20031113	(200382)*	EN	227

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003092670	A1	WO 2003-IB1686	20030417

PRIORITY APPLN. INFO: US 2002-398132P 20020723; GB 2002-10239 20020503

TI New amino methyl ketone derivatives are **bombesin** antagonists useful for the treatment of e.g. anxiety, hepatic porphyria and anorexia.

AB . . .

Analgesic; Antiemetic; Anabolic; Eating - Disorders-Gen.; Endocrine-Gen; Vasotropic.

Tests described but no biological data given.

MECHANISM OF ACTION - **Bombesin** antagonist.

USE - (I) is useful for the treatment of anxiety, panic attacks, social phobia, depression, psychoses, sleeping disorders,. . . cancer, pancreatic cancer, hepatic porphyria, gastrointestinal secretory disturbances, gastrointestinal disorders, emesis, anorexia, pain, seasonal affective disorders (SAD), feeding disorders and **sexual**

dysfunction (male **sexual dysfunction**, male **erectile dysfunction** and female **sexual dysfunction**) (claimed).

ADVANTAGE - (I) have utility in a variety of therapeutic areas, particularly female **sexual dysfunction** (FSD) especially in the FSD in female **sexual** arousal disorder (FSAD) and male **erectile dysfunction** (MED).

Dwg.0/0

TT TT: NEW AMINO METHYL KETONE DERIVATIVE **BOMBESIN** ANTAGONIST USEFUL TREAT ANXIETY HEPATO ANORECTIC.

L7 ANSWER 6 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 2
AN 2003-267866 [26] WPIDS
CR 2003-267865 [26]
AB WO2003000666 A UPAB: 20040218

NOVELTY - Piperazine compounds (I) are new.

DETAILED DESCRIPTION - Piperazine compounds of formula (IA) and (IC), their nitrogen oxides, prodrugs, salts, solvates and hydrates are new.

Y = N;

X, Z = CR;

R = H, halo, 1-4C alkyl, amino or 1-4C alkylamino;

W = oxy, thio, amino, 1-4C alkylamino or acetylamino;

R1a, R1b, R1d, R1e = T, or

R1a + R1b = T1;

T = 1-4C alkyl or 1-4C alkoxy (both optionally halo-substituted), halo, NO2, amino, 1-4C alkylamino, CN or C(O)NH2;

T1 = 5- or 6-membered fused ring;

R1c = H;

R2a, R2b = H, 1-4C alkyl or partially or fully saturated 3-6C cycloalkyl, or

R1a + R2a or R2b = T2;

T2 = 5- or 6- membered fully saturated fused ring;

n = 0-2;

R3a, R3b = H, halo or 1-4C alkyl (optionally substituted by OH, F or 1-4C alkoxy);

R4 = H, OH, 1-4C alkyl (optionally substituted by OH or CN), 1-4C alkylcarbonyl, 1-4C alkoxy, 1-4C alkoxy-carbonyl or 3-4C alkenyl, and

Q = pyridin-2-yl, pyridin-3-yl, furan-3-yl, furan-2-yl, thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, pyrrol-2-yl, pyrrol-3-yl, pyrazol-3-yl, quinolin-2-yl, quinolin-3-yl, isoquinolin-3-yl, benzofuran-2-yl, benzofuran-3-yl, isobenzofuran-3-yl, benzothiophen-2-yl, benzothiophen-3-yl, indol-2-yl, indol-3-yl, 2H-imidazol-2-yl, oxazol-2-yl, isoxazol-3-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,3,4-oxadiazol-5-yl, 1,2,4-triazol-3-yl, 1,2,3-thiadiazol-4-yl, 1,2,3-thiadiazol-5-yl, 1,3,4-thiadiazol-2-yl, 1,3,4-thiadiazol-5-yl or 1,2,4-oxathiazol-3-yl (all optionally substituted by 1-3 halo, 1-4C alkyl, CN, NO2, amino, 1-4C alkylamino or 1-4C alkoxy).

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition (C1) which comprises (IA) and excipient, diluent or carrier;

(2) a pharmaceutical composition (C2) which comprises (IB), an antiobesity agent and an excipient, diluent or carrier;

(3) treating female **sexual dysfunction** (FSD) which comprises administering (IA), (IB) or (IC).

R1a'-R1e' = H or T, or

R1a' + R1b' = T1, or

R1a' + R2a' + R2b' = T2.

ACTIVITY - Anorectic; Anabolic; Antidepressant; Neuroleptic; Antimigraine; Antialcoholic; Antismoking; Tranquilizer; Vulnerary; Nootropic; Anticonvulsant; Antiinflammatory; Cardiant; Antidiabetic; Cerebroprotective; Neuroprotective; Antiinflammatory; Antibacterial; Thrombolytic; Gynecological.

MECHANISM OF ACTION - Serotonin (5-HT) partial agonist; 5-HT antagonist; 5-HT2a partial agonist; 5-HT2a antagonist; 5-HT2c partial agonist; 5-HT2c antagonist.

In a competition binding assay using Swiss 373 mouse cells transfected with human 5-HT2c receptor against 3H-5HT using method described in Roth et al.,J. of Pharm. And Exp. Therap., 260(3),1362-1365(1992), the compounds exhibited Ki values for 5-HT2c binding of 0.1-586.5 nM.

USE - Used for treating weight loss, obesity, bulimia, premenstrual syndrome or late luteal phase syndrome, depression, atypical depression, bipolar disorders, psychoses, schizophrenia, migraine, alcoholism, tobacco abuse, panic disorder, anxiety, post-traumatic syndrome, memory loss, dementia of aging, social phobia, attention deficit hyperactivity disorder, disruptive behavior disorder, impulse control disorder, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males (e.g. male **erectile dysfunction** (MED)), **sexual dysfunction** in females (e.g. female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD) or **sexual** pain disorder), anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous system, cardiovascular disorders, gastrointestinal disorders, diabetes insipidus, and type II diabetes (all claimed). The weight loss includes reduction in calorie intake, **sexual dysfunction** in males includes premature ejaculation and **erectile** difficulty, disorders of sleep include sleep apnea, damage of CNS includes trauma, stroke, neurodegenerative diseases or toxic or infective CNS disease e.g. encephalitis or meningitis, cardiovascular disorder includes thrombosis and gastrointestinal disorder includes **dysfunction** of gastrointestinal motility.

ADVANTAGE - The compounds increase lean meat deposition and improve lean meat to fat ratio. The compounds increases leanness and/or trim unwanted fat from pet animals. For poultry and swine breeders, the method yields leaner animals that command higher scale price from the meat industry. The compounds increase genital blood flow leading to vaginal, clitoral and labial engorgement resulting in increased vaginal lubrication via plasma transudation, vaginal compliance and genital sensitivity and restoring or potentiating the normal sexual arousal response.

Dwg.0/0

ACCESSION NUMBER:	2003-267866 [26] WPIDS
CROSS REFERENCE:	2003-267865 [26]
DOC. NO. CPI:	C2003-069745
TITLE:	New piperazine compounds are serotonin modulators used for treating e.g. obesity, schizophrenia, migraine, depression and cardiovascular disorders.
DERWENT CLASS:	B02 B03 C02
INVENTOR(S):	CHIANG, Y P; DASILVA-JARDINE, P A; GARIGIPATI, R S; GUZMAN-PEREZ, A; LIU, K K; NOVOMISLE, W A; WELCH, W M
PATENT ASSIGNEE(S):	(PFIZ) PFIZER PROD INC
COUNTRY COUNT:	100
PATENT INFORMATION:	

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003000666	A1	20030103	(200326)*	EN	76

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

NO 2003005697 A 20031219 (200412)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003000666	A1	WO 2002-IB2293	20020617
NO 2003005697	A	WO 2002-IB2293	20020617
		NO 2003-5697	20031219

PRIORITY APPLN. INFO: US 2001-299953P 20010621

AB . . .

a pharmaceutical composition (C2) which comprises (IB), an antiobesity agent and an excipient, diluent or carrier;

(3) treating female **sexual dysfunction** (FSD) which comprises administering (IA), (IB) or (IC).

R1a'-R1e' = H or T, or

R1a' + R1b' = T1, or

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorder, impulse control disorder, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males (e.g. male **erectile dysfunction** (MED)), **sexual dysfunction** in females (e.g. female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD) or **sexual** pain disorder), anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . . cardiovascular disorders, gastrointestinal disorders, diabetes insipidus, and type II diabetes (all claimed). The weight loss includes reduction in calorie intake, **sexual dysfunction** in males includes premature ejaculation and **erectile** difficulty, disorders of sleep include sleep apnea, damage of CNS includes trauma, stroke, neurodegenerative diseases or toxic or infective CNS disease e.g. encephalitis or meningitis, cardiovascular disorder includes thrombosis and gastrointestinal disorder includes **dysfunction** of gastrointestinal motility.

ADVANTAGE - The compounds increase lean meat deposition and improve lean meat to fat ratio. The. . .

TECH. . .

a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or its analog, a glucocorticoid receptor agonist or antagonist, an orexin receptor. . . neurotrophic factor, a

human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, or a **neuromedin** U receptor agonist.
Preferred Method: The method further involves administering at least one additional active agent comprising an estrogen receptor modulator,. . . melanocortin enhancer, at least one neutral endopeptidase inhibitor, at least one of a phosphodiesterase inhibitor or at least one of **bombesin** receptor antagonist or modulator.

L7 ANSWER 7 OF 25 IFIPAT COPYRIGHT 2004 IFI on STN
AB The present invention is directed to beta -superfamily conotoxin peptides, derivatives or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivatives thereof and pharmaceutically acceptable salts thereof for the treatment of disorders associated with voltage-gated ion channels, ligand gated channels and other receptors. The invention is further directed to nucleic acid sequences encoding the beta -superfamily conotoxin peptides and encoding beta -superfamily conotoxin propeptides, as well as the beta -superfamily conotoxin propeptides.
CLMN 61

AN	10425798 IFIPAT;IFIUDB;IFICDB
TITLE:	BETA-SUPERFAMILY CONOTOXINS
INVENTOR(S):	Garrett; James E., Salt Lake City, UT, US Jones; Robert M., Park City, UT, US Olivera; Baldomero M., Salt Lake City, UT, US Watkins; Maren, Salt Lake City, UT, US
PATENT ASSIGNEE(S):	University of Utah Research Foundation, Salt Lake City, UT, US
AGENT:	ROTHWELL, FIGG, ERNST & MANBECK, P.C., 1425 K STREET, N.W., SUITE 800, WASHINGTON, DC, 20005, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003170222	A1	20030911
APPLICATION INFORMATION:	US 2002-58053		20020129

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2001-264323P	20010129 (Provisional)
FAMILY INFORMATION:	US 2003170222	20030911

DOCUMENT TYPE:	Utility Patent Application - First Publication
FILE SEGMENT:	CHEMICAL APPLICATION

GOVERNMENT INTEREST:
(0002) This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Md. The United States Government has certain rights in the invention.
NUMBER OF CLAIMS: 61
ACLM . . . claim 36, wherein the GPCR is selected from the group consisting of MCH2R/SLT, SP1999/P2Y12, CRTH2, NPFF1, NPFF2, HH4R, h-GPR54, CysLT2, **neuromedin** receptors, BLTR2, G2A, TA1, LTB4, ghrelin, motilin MTL-R, purinergic receptors, muscarinic receptors, ORL-1, apelin, CB1, CB2 and GPCRs of orphan. . .
. . . 41. The method of claim 32, wherein the disorder is selected from the

group consisting of inflammation, pain, diabetes, obesity, **sexual dysfunction**, acromegaly, glaucoma, cardiovascular, diabetic, retinopathy, depression, myocardial infarction, stroke, epilepsy, anorexia, wasting diseases, seborrheic dermatitis, schizophrenia, mood disorders, chemotherapeutic induced. . .
45. The method of claim 32, wherein the disorder is associated with a melanocortin system or MCR **dysfunction**.
46. The method of claim 45, wherein the disorder is selected from the group consisting of **erectile dysfunction**, obesity inflammation and melanoma.

L7 ANSWER 8 OF 25 IFIPAT COPYRIGHT 2004 IFI on STN

AB Compounds of Formula (IA) that act as 5-HT receptor ligands and their uses in the treatment of diseases linked to the activation of 5-HT2 receptors in animals are described herein.

D R A W I N G

CLMN	67
AN	10380914 IFIPAT;IFIUDB;IFICDB
TITLE:	5-HT RECEPTOR LIGANDS AND USES THEREOF
INVENTOR(S):	Chiang; Phoebe, East Lyme, CT, US DaSilva-Jardine; Paul A., Killingworth, CT, US Garigipati; Ravi S., South Glastonbury, CT, US Guzman-Perez; Angel, Stonington, CT, US Liu; Kevin K., East Lyme, CT, US Novomisle; William A., Stonington, CT, US Welch; Willard M. JR., Mystic, CT, US
PATENT ASSIGNEE(S):	Unassigned
AGENT:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003125334	A1	20030703
APPLICATION INFORMATION:	US 2002-163881		20020605

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2001-299953P	20010621 (Provisional)
FAMILY INFORMATION:	US 2003125334	20030703

DOCUMENT TYPE:	Utility Patent Application - First Publication
FILE SEGMENT:	CHEMICAL APPLICATION
NUMBER OF CLAIMS:	67

ACLM . . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.

. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid

receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist; and (ii) a pharmaceutically acceptable carrier, excipient, diluent, or a mixture thereof; and c) a container.

. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a Neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . a ciliary neurotrophic factor, an AGRP, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

60. A method for treating female **sexual dysfunction** (FSD) comprising the step of administering to a female in need thereof a therapeutically effective amount of a compound of. . .

61. A method for treating female **sexual dysfunction** (FSD) comprising the step of administering to a female in need thereof a therapeutically effective amount of a compound of. . .

. . . more of an NEP inhibitor; (8) one or more of a PDE inhibitor; and (9) one or more of a **bombesin** receptor antagonist or modulator.

65. The method of claim 60, 61, 62 or 63 wherein said FSD is female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD), or **sexual** pain disorder.
66. A method for treating male **erectile dysfunction** (MED) comprising the step of administering to a male in need thereof a therapeutically effective amount of a compound of. . .
67. A method for treating male **erectile dysfunction** (MED) comprising the step of administering to a male in need thereof a therapeutically effective amount of a compound of. . .

L7 ANSWER 9 OF 25 IFIPAT COPYRIGHT 2004 IFI on STN

AB The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor associated with male genitalia, in the preparation/manufacture of a medicament for the treatment or prevention of male **erectile dysfunction** (MED).

CLMN 44 10 Figure(s).
FIG. 1 which shows a graph;
FIG. 2 which shows a graph;
FIG. 3 which shows a graph;
FIG. 4 which shows a nucleotide sequence;
FIG. 5 which shows a nucleotide sequence;
FIG. 6 which shows a nucleotide sequence;
FIG. 7 which shows a nucleotide sequence;
FIG. 8 which shows a nucleotide sequence;
FIG. 9 which shows a nucleotide sequence;
FIG. 10 which shows a graph.

AN 10375295 IFIPAT;IFIUDB;IFICDB
TITLE: TREATMENT OF MALE **SEXUAL DYSFUNCTION**
INVENTOR(S): Naylor; Alasdair Mark, Sandwich, GB
Van Der Graaf; Pieter Hadewijn, Sandwich, GB
Wayman; Christopher Peter, Sandwich, GB
PATENT ASSIGNEE(S): Unassigned
AGENT: Gregg C. Benson Pfizer Inc., Patent Department, MS4159, Eastern Point Road, Groton, CT, 06340, US

	NUMBER	PK	DATE	
PATENT INFORMATION:	US 2003119714	A1	20030626	
APPLICATION INFORMATION:	US 2001-17273		20011212	
	APPLN. NUMBER		DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION-IN-PART OF:	US 2001-895367		20010629	
CONTINUATION-IN-PART OF:	US 2001-905846		20010713	
	NUMBER		DATE	
PRIORITY APPLN. INFO.:	GB 2000-306472		20001215	
	GB 2001-110378		20010405	
	GB 2001-87303		20010406	
	GB 2001-99100		20010423	
	GB 2001-206796		20010824	
	US 2001-265358P		20010131	(Provisional)

US 2001-291722P 20010517 (Provisional)
FAMILY INFORMATION: US 2003119714 20030626
DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
NUMBER OF CLAIMS: 44 10 Figure(s).
DESCRIPTION OF FIGURES:

FIG. 1 which shows a graph;
FIG. 2 which shows a graph;
FIG. 3 which shows a graph;
FIG. 4 which shows a nucleotide sequence;
FIG. 5 which shows a nucleotide sequence;
FIG. 6 which shows a nucleotide sequence;
FIG. 7 which shows a nucleotide sequence;
FIG. 8 which shows a nucleotide sequence;
FIG. 9 which shows a nucleotide sequence;
FIG. 10 which shows a graph.

TI TREATMENT OF MALE **SEXUAL DYSFUNCTION**

AB . . . NPY Y1 receptor associated with male genitalia, in the preparation/manufacture of a medicament for the treatment or prevention of male **erectile dysfunction** (MED).

ECLM . . . for an NPY associated with male genitalia, in the preparation of a medicament for the treatment or prevention of male **erectile dysfunction** (MED).

ACLM . . . use according to any one of the preceding claims, wherein said NPY and/or NPY Y1inhibitor is administered before and/or during **sexual** arousal.

. . . The use of an NPY Y1 inhibitor in the manufacture of a medicament for selectively increasing the intracavernosal pressure during **sexual** arousal.

11. A pharmaceutical composition for use in the treatment of male **erectile dysfunction** (MED); the pharmaceutical composition comprising an inhibitor of a neuropeptide Y (NPY), which inhibitor when in use is selective for. . .

. . . animal which method comprises delivering to an individual an NPYi that is capable of selectively increasing the intracavernosal pressure during **sexual** arousal.

. . . that can be used to treat MED, the assay comprising: determining whether a test agent can directly enhance the endogenous **erectile** process; wherein said enhancement is defined as a potentiation of intracavernosal pressure (and/or cavernosal blood flow) in the presence of. . .

. . . entity present in such an amount as to cause MED; wherein the entity has a direct effect on the endogenous **erectile** process in the corpus cavernosum of the male; and wherein said entity can be modulated to achieve a beneficial effect. . .

. . . or is in an amount so as to cause MED; wherein the entity has a direct effect on the endogenous **erectile** process and wherein said entity can be modulated to achieve a beneficial effect by use of an agent; and wherein. . .

32. An assay method for identifying an agent that can directly enhance the endogenous **erectile** process in order to treat MED, the assay method comprising: administering an agent to the animal model of claim 30 or claim 31; and measuring the change in the endogenous **erectile** process; wherein said change is defined as a potentiation of intracavernosal pressure (and/or cavernosal blood flow)

in the animal model. . .
. . . agonist or modulator for oxytocin/vasopressin receptors, preferably a selective oxytocin agonist or modulator; (xxxiv) Modulators of cannabinoid receptors; (xxxv) A **bombesin** receptor antagonist, more particularly a **bombesin** BB1, BB2, BB3, or BB4 receptor antagonist, preferably a **bombesin** BB1 inhibitor; (xxxvi) A SEP inhibitor; (xxxvii) An agent capable of modulating the activity of an intermediate conductance calcium-activated potassium (IKCa) channel in the **sexual** genitalia of an individual.

L7 ANSWER 10 OF 25 IFIPAT COPYRIGHT 2004 IFI on STN
AB Compounds of Formula (IA) that act as 5-HT receptor ligands and their uses in the treatment of diseases linked to the activation of 5-HT2 receptors in animals are described herein.

D R A W I N G

CLMN 61
AN 10360689 IFIPAT;IFIUDB;IFICDB
TITLE: 5-HT RECEPTOR LIGANDS AND USES THEREOF
INVENTOR(S): Chiang; Phoebe, East Lyme, CT, US
Novomisle; William A., Stonington, CT, US
Welch; Willard M. JR., Mystic, CT, US
PATENT ASSIGNEE(S): Unassigned
AGENT: PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003105106	A1	20030605
APPLICATION INFORMATION:	US 2002-156884		20020528

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2001-299953P	20010621 (Provisional)
FAMILY INFORMATION:	US 2003105106	20030605

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
NUMBER OF CLAIMS: 61
ACLM . . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.
. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.
. . . phobia, attention deficit hyperactivity disorder, disruptive behavior

disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist; and (ii) a pharmaceutically acceptable carrier, excipient, diluent, or a mixture thereof; and c) a container.

. . . a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a Neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . . a ciliary neurotrophic factor, an AGRP, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, and a **neuromedin** U receptor agonist.

. . . phobia, attention deficit hyperactivity disorder, disruptive behavior disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males, **sexual dysfunction** in females, anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . .

57. A method for treating female **sexual dysfunction** (FSD) comprising the step of administering to a female in need thereof a therapeutically effective amount of a compound of. . .

. . . more of an NEP inhibitor; (8) one or more of a PDE inhibitor; and (9) one or more of a **bombesin** receptor antagonist or modulator.

60. The method of claims 57, 58 or 59 wherein said FSD is female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD), or **sexual** pain disorder.

61. A method for treating male **erectile dysfunction** (MED) comprising the step of administering to a male in need thereof a therapeutically effective amount of a compound of. . .

L7 ANSWER 11 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-267865 [26] WPIDS
CR 2003-267866 [26]
AB WO2003000663 A UPAB: 20030716
NOVELTY - Piperazine compounds (I) are new.
DETAILED DESCRIPTION - Piperazine compounds of formula (IA) and (IC), their nitrogen oxides, prodrugs, salts, solvates and hydrates are new.
Z = N, and
X, Y = CR, or
X = N, and
Y, Z = CR;
R = H, halo, 1-4C alkyl, amino or 1-4C alkylamino;
W = oxy, thio, amino, 1-4C alkylamino or acetylamino;
at least one of R1a, R1b, R1d, R1e = 1-4C alkyl or 1-4C alkoxy (both optionally halo substituted), halo, NO2, NH2, CN or C(O)NH2, or
R1a + R1b = 5- or 6-membered fused ring, or
R1a + R2a or R2b = 5- or 6-membered fully saturated fused ring;
R1c = H;
R2a, R2b = H, 1-4C alkyl or partially or fully saturated 3-6C cycloalkyl;
n = 0-2;
R3a, R3b = H or 1-4C alkyl (optionally substituted by OH, F or 1-4C alkoxy);
R4a = H, OH, 1-4C alkyl (optionally substituted by OH or CN), 1-4C alkylcarbonyl, 1-4C alkoxy, 1-4C alkoxy-carbonyl or 3-4C alkenyl;
R4 = R4a or amino protecting group;
Q = pyridin-2-yl, pyridin-3-yl, furan-3-yl, furan-2-yl, thiophen-2-yl, thiophen-3-yl, thiazol-2-yl, pyrrol-2-yl, pyrrol-3-yl, pyrazol-3-yl, quinolin-2-yl, quinolin-3-yl, isoquinolin-3-yl, benzofuran-2-yl, benzofuran-3-yl, isobenzofuran-3-yl, benzothiophen-2-yl, benzothiophen-3-yl, indol-2-yl, indol-3-yl, 2H-imidazol-2-yl, oxazol-2-yl, isoxazol-3-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-triazol-3-yl or 1,2,4-oxathiazol-3-yl (all optionally substituted by 1-3 halo, 1-4C alkyl or 1-4C alkyloxy).
INDEPENDENT CLAIMS are also included for the following:
(1) a composition comprising (IA) and an excipient, diluent or carrier, and
(2) a composition comprising a piperazine compound of formula (IB), its nitrogen oxides, prodrugs, salts, solvates or hydrates, an antiobesity agent and an excipient, diluent or carrier, and
(3) treating female **sexual dysfunction** which comprises administering (IA)-(IC).
R1a'-R1e' = 1-4C alkyl or 1-4C alkoxy (both optionally halo-substituted), halo or H, and
n' = 0 or 1.
ACTIVITY - Anorectic; Anabolic; Antidepressant; Neuroleptic; Antimigraine; Antialcoholic; Antismoking; Tranquilizer; Vulnerary; Nootropic; Anticonvulsant; Antiinflammatory; Cardiant; Antidiabetic; Cerebroprotective; Neuroprotective; Antiinflammatory; Antibacterial; Thrombolytic.
MECHANISM OF ACTION - Serotonin (5-HT) partial agonist; 5-HT antagonist; 5-HT2a partial agonist; 5-HT2a partial antagonist; 5-HT2c partial agonist; 5-HT2c partial antagonist).
In a competition binding assay using Swiss 373 mouse cells transfected with human 5HT2c receptor against 3H-5HT using method described in Roth et al.,J. of Pharm. And Exp. Therap., 260(3),1362-1365(1992), the compounds exhibited Ki values for 5HT2c

binding of 0.2-238 nM.

USE - Used for treating weight loss, obesity, bulimia, premenstrual syndrome or late luteal phase syndrome, depression, atypical depression, bipolar disorders, psychoses, schizophrenia, migraine, alcoholism, tobacco abuse, panic disorder, anxiety, post-traumatic syndrome, memory loss, dementia of aging, social phobia, attention deficit hyperactivity disorder, disruptive behaviors disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males (e.g. male **erectile dysfunction** (MED)), **sexual dysfunction** in females (e.g. female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD) or **sexual** pain disorder), anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous system, cardiovascular disorders, gastrointestinal disorders, diabetes insipidus, and type II diabetes (all claimed). The weight loss includes reduction in calorie intake, **sexual dysfunction** in males includes premature ejaculation and **erectile** difficulty, disorders of sleep include sleep apnea, damage of CNS includes trauma, stroke, neurodegenerative diseases or toxic or infective CNS disease e.g. encephalitis or meningitis, cardiovascular disorder include thrombosis and gastrointestinal disorder includes **dysfunction** of gastrointestinal motility.

ADVANTAGE - The compounds increase lean meat deposition and improvement in lean meat to fat ratio. The compounds increase leanness and/or trim unwanted fat from pet animals. For poultry and swine breeders the method yields leaner animals that command higher scale price from the meat industry. The compounds increase genital blood flow leading to vaginal, clitoral and labial engorgement resulting in increased vaginal lubrication via plasma transudation, vaginal compliance and genital sensitivity and restore or potentiate the normal **sexual** arousal response.

Dwg.0/0

ACCESSION NUMBER: 2003-267865 [26] WPIDS
CROSS REFERENCE: 2003-267866 [26]
DOC. NO. CPI: C2003-069744
TITLE: New piperazine compounds are serotonin 5-HT receptor modulators used for treating e.g. obesity, migraine, schizophrenia and depression.
DERWENT CLASS: B02 B03
INVENTOR(S): CHIANG, P; NOVOMISLE, W A; WELCH, W M; DASILVA-JARDINE, P A; GARIGIPATI, R S; GUZMAN-PEREZ, A; LIU, K K; CHIANG, Y P
PATENT ASSIGNEE(S): (CHIA-I) CHIANG P; (NOVO-I) NOVOMISLE W A; (WELC-I) WELCH W M; (DASI-I) DASILVA-JARDINE P A; (GARI-I) GARIGIPATI R S; (GUZM-I) GUZMAN-PEREZ A; (LIUK-I) LIU K K; (PFIZ) PFIZER PROD INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003000663	A1	20030103	(200326)*	EN	56

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW
US 2003105106 A1 20030605 (200339)
US 2003125334 A1 20030703 (200345)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003000663 A1		WO 2002-IB2261	20020617
US 2003105106 A1	Provisional	US 2001-299953P	20010621
		US 2002-156884	20020528
US 2003125334 A1	Provisional	US 2001-299953P	20010621
		US 2002-163881	20020605

PRIORITY APPLN. INFO: US 2001-299953P 20010621; US 2002-156884 20020528; US 2002-163881 20020605

AB . . .
nitrogen oxides, prodrugs, salts, solvates or hydrates, an antiobesity agent and an excipient, diluent or carrier, and

(3) treating female **sexual dysfunction** which comprises administering (IA)-(IC).

R1a'-R1e' = 1-4C alkyl or 1-4C alkoxy (both optionally halo-substituted), halo or H, and

n' = 0. . . phobia, attention deficit hyperactivity disorder, disruptive behaviors disorders, impulse control disorders, borderline personality disorder, obsessive compulsive disorder, chronic fatigue syndrome, **sexual dysfunction** in males (e.g. male **erectile dysfunction** (MED)), **sexual dysfunction** in females (e.g. female **sexual** arousal disorder (FSAD), female orgasmic disorder (FOD), hypoactive **sexual** desire disorder (HSDD) or **sexual** pain disorder), anorexia nervosa, disorders of sleep, autism, seizure disorders, epilepsy, mutism, spinal cord injury, damage of the central nervous. . . cardiovascular disorders, gastrointestinal disorders, diabetes insipidus, and type II diabetes (all claimed). The weight loss includes reduction in calorie intake, **sexual dysfunction** in males includes premature ejaculation and **erectile** difficulty, disorders of sleep include sleep apnea, damage of CNS includes trauma, stroke, neurodegenerative diseases or toxic or infective CNS disease e.g. encephalitis or meningitis, cardiovascular disorder include thrombosis and gastrointestinal disorder includes **dysfunction** of gastrointestinal motility.

ADVANTAGE - The compounds increase lean meat deposition and improvement in lean meat to fat ratio.. . . engorgement resulting in increased vaginal lubrication via plasma transudation, vaginal compliance and genital sensitivity and restore or potentiate the normal **sexual** arousal response.

Dwg.0/0

TECH. . .
a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or its analog, a glucocorticoid receptor

agonist or antagonist, an orexin receptor. . . neurotrophic factor, a human agouti-related protein, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or reverse agonist, or a **neuromedin** U receptor agonist.
Preferred Method: The method also comprises administering at least one additional active agent comprising an estrogen receptor modulator,. . . enhancer, at least one neutral endopeptidase inhibitor, or at least one of a phosphodiesterase inhibitor or at least one of **bombesin** receptor antagonist or modulator.

L7 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

AB **Bombesin** receptor antagonists (Ar)r-(CH2)j-(X)q-(CH2)kNR3CR5(CH2Ar1)CONR4(CH2)l(CR1R6)m(CH2)nR2 [j, n = 0-2; k, m, q, r = 0 or 1; l = 0-3 (when r = 0, Ar is replaced by H); Ar = (un)substituted Ph, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl or thiazolyl; Ar1 = any group for Ar or indolyl or pyridyl N-oxide; R1 = H, alkyl, (oxa, aza)cycloalkyl; R6 = H, Me or together with R6 forms a carbonyl group or a ring which can contain an oxygen or nitrogen atom; R3-R5 = H, alkyl; R2 = H, OH, alkoxy, NMe2, carbamoyl or certain ring structures; X is a divalent radical derived from isoxazole, pyridine, pyridazine, pyrimidine, etc.] or their pharmaceutically acceptable salts were prepared The compds. of the invention have an affinity for the BB1 receptor and some of them also have affinity for the BB2 receptor. Accordingly they may be useful for the diagnosis, prevention, or treatment of male and female **sexual dysfunction**. Thus, (S)-3-(1H-indol-3-yl)-N-[1-(5-methoxypyridin-2-yl)cyclohexylmethyl]-2-methyl-2-[4-(4-nitrophenyl)oxazol-2-ylamino]propionamide (1) was prepared via amidation reaction and showed Ki = 4 or 24 nM in the BB1 and BB2 binding assay, resp. Compound 1 was also assayed for female rat **sexual** proceptivity.

ACCESSION NUMBER: 2002:391709 CAPLUS
DOCUMENT NUMBER: 136:386398
TITLE: Preparation of **bombesin** receptor antagonists
INVENTOR(S): Higginbottom, Michael; Pritchard, Martyn Clive; Stock, Herman Thijs
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040475	A1	20020523	WO 2001-EP14402	20011116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2369118	A1	20020522	GB 2000-28146	20001117
AU 2002017095	A5	20020527	AU 2002-17095	20011116
EP 1334102	A1	20030813	EP 2001-996539	20011116

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: GB 2000-28146 A 20001117
WO 2001-EP14402 W 20011116

OTHER SOURCE(S): MARPAT 136:386398
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of **bombesin** receptor antagonists

AB **Bombesin** receptor antagonists (Ar)r-(CH2)j-(X)q-(CH2)kNR3CR5(CH2Ar1)CONR4(CH2)l(CR1R6)m(CH2)nR2 [j, n = 0-2; k, m, q, r = 0 or 1; l = 0-3 (when r = 0, Ar is replaced by H); Ar = (un)substituted Ph, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl or thiazolyl; Ar1 = any group for Ar or indolyl or pyridyl N-oxide; R1 = H, alkyl, (oxa, aza)cycloalkyl; R6 = H, Me or together with R6 forms a carbonyl group or a ring which can contain an oxygen or nitrogen atom; R3-R5 = H, alkyl; R2 = H, OH, alkoxy, NMe2, carbamoyl or certain ring structures; X is a divalent radical derived from isoxazole, pyridine, pyridazine, pyrimidine, etc.] or their pharmaceutically acceptable salts were prepared The compds. of the invention have an affinity for the BB1 receptor and some of them also have affinity for the BB2 receptor. Accordingly they may be useful for the diagnosis, prevention, or treatment of male and female **sexual dysfunction**. Thus, (S)-3-(1H-indol-3-yl)-N-[1-(5-methoxypyridin-2-yl)cyclohexylmethyl]-2-methyl-2-[4-(4-nitrophenyl)oxazol-2-ylamino]propionamide (1) was prepared via amidation reaction and showed Ki = 4 or 24 nM in the BB1 and BB2 binding assay, resp. Compound 1 was also assayed for female rat **sexual** proceptivity.

ST **bombesin** receptor antagonist amino acid deriv prepn; **sexual dysfunction** treatment **bombesin** receptor antagonist amino acid prepn

IT Intestine, disease
(Crohn's; preparation of **bombesin** receptor antagonists)

IT Mental disorder
(affective, seasonal; preparation of **bombesin** receptor antagonists)

IT Intestine, disease
(colitis; preparation of **bombesin** receptor antagonists)

IT Mental disorder
(depression; preparation of **bombesin** receptor antagonists)

IT Appetite
Sexual behavior
Sleep
(disorder; preparation of **bombesin** receptor antagonists)

IT Porphyria
(hepatic; preparation of **bombesin** receptor antagonists)

IT Intestine, disease
(inflammatory; preparation of **bombesin** receptor antagonists)

IT Mental disorder
(phobia; preparation of **bombesin** receptor antagonists)

IT Anorexia
Antitumor agents
Anxiolytics
Digestive tract, disease
Human
Lung, disease
Pain
Pruritus
Vomiting

(preparation of **bombesin** receptor antagonists)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of **bombesin** receptor antagonists)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **bombesin** receptor antagonists)

IT Mental disorder
(psychosis; preparation of **bombesin** receptor antagonists)

IT Hypertension
(pulmonary; preparation of **bombesin** receptor antagonists)

IT Memory, biological
(retention defect; preparation of **bombesin** receptor antagonists)

IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P 425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P 425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 426267-06-3P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **bombesin** receptor antagonists)

IT 99-81-0 108-86-1, Bromobenzene, reactions 122-78-1, Phenylacetaldehyde 555-16-8, 4-Nitrobenzaldehyde, reactions 591-17-3, 1-Bromo-3-methylbenzene 613-89-8, 2-Aminoacetophenone 615-18-9, 2-Chlorobenzoxazole 673-06-3, D-Phenylalanine 931-97-5, 1-Hydroxycyclohexanecarbonitrile 1532-97-4, 4-Bromoisoquinoline 2052-07-5, 2-Bromobiphenyl 2104-06-5 4265-16-1, Benzofuran-2-carboxaldehyde 4595-59-9, 5-Bromopyrimidine 7693-46-1, p-Nitrophenyl chloroformate 16709-25-4 19524-06-2, 4-Bromopyridine hydrochloride 39774-26-0, 2-Bromo-6-phenylpyridine 142854-50-0 204067-08-3 204067-12-9 425641-35-6 425641-36-7 425641-37-8 425641-38-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **bombesin** receptor antagonists)

IT 105754-24-3P 204067-15-2P 204067-16-3P 204067-17-4P 425641-31-2P 425641-32-3P 425641-33-4P 425641-34-5P 425641-39-0P 425641-40-3P 425641-42-5P 425641-43-6P 425641-45-8P 426267-07-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **bombesin** receptor antagonists)

L7 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females.

ACCESSION NUMBER: 2002:368981 CAPLUS
DOCUMENT NUMBER: 136:380137
TITLE: **Bombesin** receptor antagonists, and preparation thereof, for the treatment of **sexual dysfunction**
INVENTOR(S): Gonzalez, Maria Isabel; Pinnock, Robert Denham; Pritchard, Martyn Clive
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 72 pp., Cont.-in-part of U. S. Ser. No. 700,165.
CODEN: USXXCO

09/700,165

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002058606	A1	20020516	US 2001-759777	20010112
US 2002169101	A1	20021114	US 2001-999284	20011115

PRIORITY APPLN. INFO.:

US 1999-133355P	P	19990510
WO 2000-GB1787	W	20000510
US 2000-700165	A2	20001109
US 2001-759777	A2	20010112
GB 2001-9910	A	20010423
GB 2001-11037	A	20010504

TI **Bombesin** receptor antagonists, and preparation thereof, for the treatment of **sexual dysfunction**

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females.

ST **bombesin** receptor antagonist prepn **sexual dysfunction**

IT Behavior
(arousal; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT Aging, animal
Human
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT Vasodilators
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT **Gastrin-releasing peptide** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT **Sexual** behavior
(disorder; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT Drug delivery systems
(oral; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT Drugs
(**sexual dysfunction** induced by; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

DELACROIX

IT Pain
(**sexual** pain disorder; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agents promoting production of; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 50-28-2, Estradiol, biological studies 57-83-0, Progesterone, biological studies 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P
425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P
425639-10-7P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P
425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 425639-35-6P
425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P 425639-45-8P
425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P 425639-52-7P
425639-53-8P 425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P
425639-63-0P 425639-65-2P 425639-68-5P 425639-70-9P 425639-72-1P
425639-74-3P 425639-76-5P 425639-77-6P 425639-79-8P 425639-81-2P
425639-83-4P 425639-85-6P 425639-87-8P 425639-89-0P 425639-91-4P
425639-93-6P 425639-95-8P 425639-96-9P 425639-97-0P 425639-98-1P
425639-99-2P 425640-00-2P 425640-01-3P 425640-02-4P 425640-03-5P
425640-04-6P 425640-06-8P 425640-08-0P 425640-09-1P 425640-10-4P
425640-11-5P 425640-12-6P 425640-14-8P 425640-15-9P 425640-17-1P
425640-18-2P 425640-20-6P 425640-21-7P 425640-23-9P 425640-24-0P
425640-26-2P 425640-28-4P 425640-30-8P 425640-32-0P 425640-34-2P
425640-36-4P 425640-38-6P 425640-39-7P 425640-40-0P 425640-41-1P
425640-43-3P 425640-45-5P 425640-47-7P 425640-49-9P 425640-51-3P
425640-53-5P 425640-55-7P 425640-57-9P 425640-59-1P 425640-60-4P
425640-62-6P 425640-64-8P 425640-66-0P 425640-68-2P 425640-70-6P
425640-72-8P 425640-74-0P 425640-76-2P 425640-78-4P 425640-80-8P
425640-82-0P 425640-83-1P 425640-84-2P 425640-85-3P 425640-86-4P
425640-87-5P 425640-88-6P 425640-89-7P 425640-90-0P 425640-91-1P
425640-92-2P 425640-93-3P 425640-94-4P 425640-95-5P 425640-96-6P
425640-97-7P 425640-98-8P 425640-99-9P 425641-00-5P 425641-01-6P
425641-02-7P 425641-03-8P 425641-04-9P 425641-05-0P 425641-06-1P
425641-07-2P 425641-08-3P 425641-09-4P 425641-10-7P 425641-11-8P
425641-12-9P 425641-13-0P 425641-14-1P 425641-15-2P 425641-16-3P
425641-17-4P 425641-18-5P 425641-19-6P 425641-20-9P 425641-21-0P
425641-22-1P 425641-23-2P 425641-24-3P 425641-25-4P 425641-26-5P
425641-27-6P 425641-28-7P 425641-29-8P 425641-30-1P 426213-31-2P
426213-32-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 50-60-2, Phentolamine 745-65-3, Alprostadil 139755-83-2, Sildenafil 204067-01-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 31362-50-2, **Bombesin** 37221-79-7, Vasoactive intestinal peptide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 9068-52-4, Phosphodiesterase V
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 25506-37-0P 31558-54-0P 63430-65-9P 73717-05-2P 97534-88-8P 97557-59-0P 105754-24-3P 137140-98-8P 149358-14-5P 158556-65-1P 158951-86-1P 159672-85-2P 159672-86-3P 160233-08-9P 172154-13-1P 172154-15-3P 172154-17-5P 172154-18-6P 204067-15-2P 204067-16-3P 204067-17-4P 291761-10-9P 425641-31-2P 425641-32-3P 425641-33-4P 425641-39-0P 425641-45-8P 425641-46-9P 425641-47-0P 425641-48-1P 425641-49-2P 425641-50-5P 425641-51-6P 425641-52-7P 425641-53-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid 65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid 85-46-1, Naphthalene-1-sulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2 93-03-8 93-11-8, Naphthalene-2-sulfonyl chloride 93-25-4, (2-Methoxy-phenyl)-acetic acid 98-31-7, 3,4-Dichlorobenzenesulfonyl chloride 98-59-9, 4-Methyl-benzenesulfonyl chloride 98-60-2, 4-Chlorobenzenesulfonyl chloride 98-74-8, 4-Nitrobenzenesulfonyl chloride 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0 99-94-5, 4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8, (4-Methoxy-phenyl)-acetic acid 105-13-5, (4-Methoxyphenyl)methanol 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7, 3-Nitrobenzenesulfonyl chloride 122-78-1, Benzeneacetaldehyde 156-38-7, (4-Hydroxy-phenyl)acetic acid 349-75-7 349-88-2, 4-Fluorobenzenesulfonyl chloride 349-95-1 445-29-4, 2-Fluorobenzoic acid 446-51-5 451-82-1, (2-Fluoro-phenyl)acetic acid 488-93-7, Furan-3-carboxylic acid 527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid 552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions 579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid 587-03-1, m-Tolylmethanol 589-18-4 591-17-3, 1-Bromo-3-methylbenzene 605-65-2,

5-Dimethylaminonaphthalene-1-sulfonyl chloride 610-16-2, 2-Dimethylaminobenzoic acid 612-16-8 613-89-8 615-18-9, 2-Chlorobenzoxazole 619-25-0 619-73-8, (4-Nitrophenyl)methanol 621-36-3, m-Tolylacetic acid 621-37-4, (3-Hydroxy-phenyl)acetic acid 622-47-9, p-Tolylacetic acid 644-36-0, o-Tolylacetic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 776-04-5, 2-Trifluoromethylbenzenesulfonyl chloride 777-44-6, 3-Trifluoromethylbenzenesulfonyl chloride 873-76-7, (4-Chlorophenyl)methanol 874-97-5 877-65-6, (4-tert-Butylphenyl)methanol 879-65-2, Quinoxaline-2-carboxylic acid 934-60-1, 6-Methyl-pyridine-2-carboxylic acid 1477-50-5, 1H-Indole-2-carboxylic acid 1592-38-7, 2-Naphthalenemethanol 1656-44-6, 2,4-Dinitrobenzenesulfonyl chloride 1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8 1805-32-9 1877-72-1, 3-Cyanobenzoic acid 1899-93-0, 3-Methylbenzenesulfonyl chloride 1918-79-2, 5-Methyl-thiophene-2-carboxylic acid 1939-99-7, Phenylmethanesulfonyl chloride 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6, Biphenyl-2-sulfonyl chloride 2766-74-7, 5-Chlorothiophene-2-sulfonyl chloride 2888-06-4, 3-Chlorobenzenesulfonyl chloride 2905-21-7, 2-Fluorobenzenesulfonyl chloride 2905-23-9, 2-Chloro-benzenesulfonyl chloride 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3405-77-4, 5-Methyl-isoxazole-3-carboxylic acid 3622-35-3, Benzothiazole-6-carboxylic acid 3740-52-1, (2-Nitro-phenyl)-acetic acid 4052-30-6, 4-Methanesulfonylbenzoic acid 4254-29-9, Indan-2-ol 4265-16-1, Benzofuran 2-carbaldehyde 4533-95-3, 2-Chloro-5-nitrobenzenesulfonyl chloride 4533-96-4, 4-Chloro-2-nitrobenzenesulfonyl chloride 4780-79-4, 1-Naphthalenemethanol 5345-27-7, 3-Methylsulfonylbenzoic acid 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2, 3-Thiopheneacetic acid 6973-60-0 7693-46-1, 4-Nitrophenyl chloroformate 10130-74-2, 3-Methoxybenzenesulfonyl chloride 10333-68-3, 2-Pyrrol-1-yl-benzoic acid 13826-35-2, (3-Phenoxyphenyl)methanol 15084-51-2, 4-tert-Butylbenzenesulfonyl chloride 16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9, Thiophene-2-sulfonyl chloride 16709-25-4 17078-28-3, (4-Dimethylamino-phenyl)-acetic acid 17849-38-6, (2-Chlorophenyl)methanol 18704-37-5, Quinoline-8-sulfonyl chloride 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 23806-24-8, 3-Methyl-thiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-carboxylic acid 24424-99-5, Di-tert-butyl dicarbonate 24974-75-2, (2-Nitrophenyl)methanesulfonyl chloride 26638-43-7, 2-Chlorosulfonylbenzoic acid methyl ester 28286-86-4, 2,4-Dichloro-5-methylbenzenesulfonyl chloride 38594-42-2 39774-26-0, 2-Bromo-6-phenylpyridine 39982-49-5, 7-Quinolinemethanol 42413-03-6, 3-Chloro-4-methylbenzenesulfonyl chloride 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51527-73-2, 2,4,6-Trichlorobenzenesulfonyl chloride 54997-92-1, 4-Butylbenzenesulfonyl chloride 56542-67-7, 3-Cyanobenzenesulfonyl chloride 56946-83-9, 2,5-Dichlorothiophene-3-sulfonyl chloride 59337-92-7 69360-26-5, 2-Cyanobenzenesulfonyl chloride 71648-21-0 73713-79-8 80466-79-1, 3,5-Dimethyl-isoxazole-4-sulfonyl chloride 82964-91-8, 4-Methanesulfonylbenzenesulfonyl chloride 88398-93-0, 5-Chloro-1,3-dimethyl-1H-pyrazole-4-sulfonyl chloride 91170-93-3, 3-Chloro-4-fluoro-benzenesulfonyl chloride 94108-56-2, 4-Trifluoromethoxybenzenesulfonyl chloride 99924-18-2 114322-14-4, 2,1,3-Benzoxadiazole-4-sulfonyl chloride 137049-00-4, 1-Methyl-1H-imidazole-4-sulfonyl chloride 137049-02-6,

1,2-Dimethyl-1H-imidazole-4-sulfonyl chloride 142854-50-0 151858-64-9 160233-27-2, 5-Isoxazol-3-yl-thiophene-2-sulfonyl chloride 166964-37-0, 5-Benzenesulfonylthiophene-2-sulfonyl chloride 185908-35-4 204067-08-3 204067-12-9 206262-15-9 206262-83-1 216394-05-7 216394-11-5, 2-Methoxy-4-methylbenzenesulfonyl chloride 425641-34-5 425641-35-6 425641-36-7 425641-37-8 425641-38-9 425641-40-3 425641-41-4 425641-42-5 425641-43-6 425641-44-7 426213-33-4 426213-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **bombesin** receptor antagonists, preparation, and use for **sexual dysfunction** treatment, alone or with other agents)

L7 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. Preparation of compds. of the invention is included.

ACCESSION NUMBER: 2002:391535 CAPLUS
DOCUMENT NUMBER: 136:380143
TITLE: Treatment of **sexual dysfunction** using **bombesin** antagonist
INVENTOR(S): Gonzalez, Maria Isabel; Higginbottom, Michael; Pinnock, Robert Denham; Pritchard, Martyn Clive; Stock, Herman Thijs
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040022	A1	20020523	WO 2000-GB4380	20001117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001014046	A5	20020527	AU 2001-14046	20001117
EP 1333829	A1	20030813	EP 2000-976165	20001117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000017374	A	20030930	BR 2000-17374	20001117
WO 2002040008	A2	20020523	WO 2001-GB5018	20011114
WO 2002040008	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002023802	A5	20020527	AU 2002-23802	20011114	
EP 1333824	A2	20030813	EP 2001-994552	20011114	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001015364	A	20030923	BR 2001-15364	20011114	

PRIORITY APPLN. INFO.:

WO 2000-GB4380	A	20001117
GB 2001-9910	A	20010423
GB 2001-11037	A	20010504
WO 2001-GB5018	W	20011114

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Treatment of **sexual dysfunction** using **bombesin** antagonist

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. Preparation of compds. of the invention is included.

ST **bombesin** antagonist prepn **sexual dysfunction** treatment

IT Aging, animal
Human
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT **Bombesin** receptors
Sex hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT Neurotransmitter agonists
Neurotransmitter antagonists
Vasodilators
(**bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT Androgens
Estrogens
Hormones, animal, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT Drug delivery systems
(capsules; **bombesin** antagonists for treatment of **sexual dysfunction**)

IT **Sexual** behavior
(disorder; **bombesin** antagonists for treatment of **sexual dysfunction**)

IT Drugs
(drug-induced **sexual dysfunction**; **bombesin** antagonists for treatment of **sexual dysfunction**)

IT Drug delivery systems
(elixirs; **bombesin** antagonists for treatment of

sexual dysfunction)
IT Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormones, and steroid hormone modulators; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)
IT Metabolism
(monoamine synthesis, metabolism, and uptake modifiers; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)
IT Monoamines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoamine synthesis, metabolism, and uptake modifiers; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)
IT Drug delivery systems
(ointments, creams; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(oral; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(powders; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Analgesics
(**sexual** pain disorder; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(steroid, and steroid hormone modulators; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)
IT Drug delivery systems
(suppositories, vaginal; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(suppositories; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(syrups; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(tablets; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(transdermal; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Drug delivery systems
(unit doses; **bombesin** antagonists for treatment of **sexual dysfunction**)
IT Biological transport

(uptake, monoamine synthesis, metabolism, and uptake modifiers; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agents promoting production of; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT 425640-90-0P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 50-28-2, Estradiol, biological studies 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 57-83-0, Progesterone, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P
425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P
425639-10-7P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P
425639-28-7P 425639-31-2P 425639-33-4P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 50-50-0, Estradiol benzoate 102577-19-5, **Neuromedin** B
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 425639-35-6P 425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P
425639-45-8P 425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P
425639-53-8P 425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P
425639-65-2P 425639-68-5P 425639-70-9P 425639-72-1P 425639-74-3P
425639-76-5P 425639-77-6P 425639-79-8P 425639-81-2P 425639-83-4P
425639-85-6P 425639-87-8P 425639-89-0P 425639-91-4P 425639-93-6P
425639-95-8P 425639-96-9P 425639-97-0P 425639-98-1P 425639-99-2P
425640-00-2P 425640-01-3P 425640-02-4P 425640-03-5P 425640-04-6P
425640-06-8P 425640-08-0P 425640-09-1P 425640-10-4P 425640-11-5P
425640-12-6P 425640-14-8P 425640-15-9P 425640-17-1P 425640-18-2P
425640-20-6P 425640-21-7P 425640-23-9P 425640-24-0P 425640-26-2P
425640-28-4P 425640-30-8P 425640-32-0P 425640-34-2P 425640-36-4P
425640-38-6P 425640-39-7P 425640-40-0P 425640-41-1P 425640-43-3P
425640-45-5P 425640-47-7P 425640-49-9P 425640-51-3P 425640-53-5P
425640-55-7P 425640-57-9P 425640-59-1P 425640-60-4P 425640-62-6P
425640-64-8P 425640-66-0P 425640-68-2P 425640-70-6P 425640-72-8P
425640-74-0P 425640-76-2P 425640-78-4P 425640-80-8P 425640-82-0P
425640-83-1P 425640-84-2P 425640-85-3P 425640-86-4P 425640-87-5P
425640-88-6P 425640-89-7P 425640-91-1P 425640-92-2P 425640-93-3P

425640-94-4P 425640-95-5P 425640-96-6P 425640-97-7P 425640-98-8P
425640-99-9P 425641-00-5P 425641-01-6P 425641-02-7P 425641-03-8P
425641-04-9P 425641-05-0P 425641-06-1P 425641-07-2P 425641-08-3P
425641-09-4P 425641-10-7P 425641-11-8P 425641-12-9P 425641-13-0P
425641-14-1P 425641-15-2P 425641-16-3P 425641-17-4P 425641-18-5P
425641-19-6P 425641-20-9P 425641-21-0P 425641-22-1P 425641-23-2P
425641-24-3P 425641-25-4P 425641-26-5P 425641-27-6P 425641-28-7P
425641-29-8P 425641-30-1P 426213-31-2P 426213-32-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 204067-01-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**)

IT 50-49-7, Imipramine 50-60-2, Phentolamine 745-65-3, Alprostadil 7424-00-2, p-Chlorophenylalanine 87051-43-2, Ritanserin 97466-90-5, Quinelorane 139755-83-2, Sildenafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT 37221-79-7, Vasoactive intestinal polypeptide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT 9068-52-4, Phosphodiesterase V
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **bombesin** antagonists for treatment of **sexual dysfunction**, and use with other agents)

IT 25506-37-0P 31558-54-0P 63430-65-9P 73717-05-2P 97534-88-8P 97557-59-0P 105754-24-3P 137140-98-8P 149358-14-5P 158556-65-1P 158951-86-1P 159672-85-2P 159672-86-3P 160233-08-9P 172154-13-1P 172154-15-3P 172154-17-5P 172154-18-6P 204067-15-2P 204067-16-3P 204067-17-4P 291761-10-9P 425641-31-2P 425641-32-3P 425641-33-4P 425641-34-5P 425641-39-0P 425641-45-8P 425641-46-9P 425641-47-0P 425641-48-1P 425641-49-2P 425641-50-5P 425641-51-6P 425641-52-7P 425641-53-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; **bombesin** antagonists for treatment of **sexual dysfunction**)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid 65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid 85-46-1, 1-Naphthalenesulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2 93-03-8 93-11-8, 2-Naphthalenesulfonyl chloride 93-25-4, (2-Methoxyphenyl)acetic acid 98-31-7 98-59-9 98-60-2 98-74-8 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0 99-94-5, 4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8, (4-Methoxyphenyl)acetic acid 105-13-5 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7 122-78-1, Benzeneacetaldehyde 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7 349-88-2 349-95-1

445-29-4, 2-Fluorobenzoic acid 446-51-5 451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid 527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid 552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions 579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid 587-03-1 589-18-4 591-17-3, 1-Bromo-3-methylbenzene 605-65-2 610-16-2, 2-Dimethylaminobenzoic acid 612-16-8 613-89-8 615-18-9, 2-Chlorobenzoxazole 619-25-0 619-73-8 621-36-3, m-Tolylacetic acid 621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid 644-36-0, o-Tolylacetic acid 701-27-9 776-04-5 777-44-6 873-76-7 874-97-5 877-65-6 879-65-2, Quinoxaline-2-carboxylic acid 931-97-5, 1-Hydroxycyclohexanecarbonitrile 934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5, 1H-Indole-2-carboxylic acid 1592-38-7, 2-Naphthalenemethanol 1656-44-6 1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8 1805-32-9 1877-72-1, 3-Cyanobenzoic acid 1899-93-0 1918-79-2, 5-Methylthiophene-2-carboxylic acid 1939-99-7, Benzenemethanesulfonyl chloride 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6, [1,1'-Biphenyl]-2-sulfonyl chloride 2766-74-7 2888-06-4 2905-21-7 2905-23-9 2991-42-6 3405-77-4, 5-Methylisoxazole-3-carboxylic acid 3622-35-3, Benzothiazole-6-carboxylic acid 3740-52-1, (2-Nitrophenyl)acetic acid 4052-30-6, 4-Methanesulfonylbenzoic acid 4254-29-9 4265-16-1, Benzofuran-2-carbaldehyde 4533-95-3 4533-96-4 4780-79-4, 1-Naphthalenemethanol 5345-27-7 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2, 3-Thiopheneacetic acid 6973-60-0 7693-46-1, p-Nitrophenyl chloroformate 10130-74-2 10333-68-3, 2-Pyrrol-1-yl benzoic acid 13826-35-2 15084-51-2 16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9, 2-Thiophenesulfonyl chloride 16709-25-4 17078-28-3, (4-Dimethylaminophenyl)acetic acid 17849-38-6 18704-37-5, 8-Quinolinesulfonyl chloride 23095-31-0 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-carboxylic acid 24424-99-5, Di-tert-butyl dicarbonate 24974-75-2 26638-43-7 28286-86-4 38594-42-2 39774-26-0, 2-Bromo-6-phenylpyridine 42413-03-6 49584-26-1 51527-73-2 54997-92-1 56542-67-7 56946-83-9 59337-92-7 69360-26-5 71648-21-0 80466-79-1 82964-91-8 88398-93-0 91170-93-3 94108-56-2 99924-18-2 100516-88-9, 6-Quinolinemethanol 114322-14-4, 2,1,3-Benzoxadiazole-4-sulfonyl chloride 137049-00-4 137049-02-6 142854-50-0 151858-64-9 160233-27-2 166964-37-0 166964-39-2, 1,2,5-Thiadiazole-3-sulfonyl chloride 185908-35-4 204067-08-3 204067-12-9 206262-15-9 206262-83-1 216394-05-7 216394-11-5 425639-25-4 425641-35-6 425641-36-7 425641-37-8 425641-38-9 425641-40-3 425641-41-4 425641-42-5 425641-43-6 426213-33-4 426213-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **bombesin** antagonists for treatment of **sexual dysfunction**)

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AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compounds, for example PDE5 inhibitors, NEP inhibitors and lasofoxifene.

CLMN 67 26 Figure(s).

FIG. 1: Effect of (S) 3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)propionamide (Compound (1)) on female rat **sexual** proceptivity.

FIG. 2: Effect of Compound (1) on female rat **sexual** receptivity.

FIG. 3: Effect of repeated administration of Compound (1) on female rat proceptivity.

FIG. 4: Effect of intracerebroventricular administration of Compound (1) on female rat **sexual** proceptivity.

FIG. 5: Inhibitory effect of NMB on female rat **sexual** proceptivity and antagonism of this effect by Compound (1).

FIG. 6: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through progesterone.

FIG. 7: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through oestradiol.

FIG. 8: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through prolactin.

FIG. 9: Results of an investigation to show whether the effect of Compound on female **sexual** behaviour is mediated through LH.

FIG. 10: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through FSH.

FIG. 11: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Mount Latency).

FIG. 12: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Intromission Latency).

FIG. 13: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Number of Mounts+Intromission).

FIG. 14: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Ejaculation Latency).

FIG. 15: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Refractory Period).

FIG. 16: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (Mount Latency).

FIG. 17: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (Ejaculation Latency).

FIG. 18: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (% animals ejaculating).

FIG. 19: Effect of (S)-3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2ylamino)-propionamide (Compound (2)) in PEG 200 on female rat **sexual** proceptivity.

FIG. 20: Effect of Compound (2) in methylcellulose on female rat **sexual** proceptivity.

FIG. 21: Effect of Compound (2) in PEG 200 on female rat **sexual** receptivity.

FIG. 22: Effect of compound 1 on basal and pelvic nervestimulated increases in female genital blood flow in the anaesthetised rabbit model of female **sexual** arousal.

FIG. 23: Effect of (2S)-N-((1-(4-aminophenyl)cyclohexyl)methyl)3-(1H-indol-3-yl)-2-methyl-2-(((4-nitroanilino)carbonyl)amino) propanamide (Compound 3) on basal and pelvic nerve-stimulated increases female genital blood flow in the anaesthetised rabbit model of female **sexual** arousal.

FIG. 24: Effect of compound 1 on penile intracavemosal pressure in the

conscious male rat.
FIG. 25: Effect of compound 3 on penile intracavernosal pressure in the conscious male rat model of penile erection.
FIG. 26: Effect of compound 3 alone and in combination with a phosphodiesterase type five inhibitor on basal and pelvic nervestimulated increases penile intracavernosal pressure in the anaesthetised rabbit model of penile erection.

AN 10225394 IFIPAT;IFIUDB;IFICDB
TITLE: TREATMENT OF **SEXUAL DYSFUNCTION**
INVENTOR(S): Gonzalez; Maria Isabel, Cambridge, GB
Higginbottom; Michael, Cambridge, GB
Naylor; Alisdair Mark, Kent, GB
Pinnock; Robert Denham, Cambridgshire, GB
Pritchard; Martyn Clive, Huntingdon, GB
Stock; Herman Thijs, Wijchen, NL
Van Der Graaf; Pieter Hadewijn, Kent, GB
Wayman; Christopher Peter, Kent, GB
PATENT ASSIGNEE(S): Unassigned
AGENT: WARNER-LAMBERT COMPANY, 2800 PLYMOUTH ROAD, ANN ARBOR, MI, 48107, US

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APPLICATION INFORMATION:	US 2001-999284		20011115

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Section 371 PCT Filing of:	WO 2000-GB1787	20000510	UNKNOWN
CONTINUATION-IN-PART OF:	US 2000-700165	20001109	PENDING
CONTINUATION-IN-PART OF:	US 2001-759777	20010112	PENDING

	NUMBER	DATE	
PRIORITY APPLN. INFO.:	GB 2001-99100	20010423	
	GB 2001-110378	20010504	
	US 1999-133355P	19990510	(Provisional)
FAMILY INFORMATION:	US 2002169101	20021114	

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
OTHER SOURCE: CA 137:372337
NUMBER OF CLAIMS: 67 26 Figure(s).
DESCRIPTION OF FIGURES:
FIG. 1: Effect of (S) 3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)propionamide (Compound (1)) on female rat **sexual** proceptivity.
FIG. 2: Effect of Compound (1) on female rat **sexual** receptivity.
FIG. 3: Effect of repeated administration of Compound (1) on female rat proceptivity.
FIG. 4: Effect of intracerebroventricular administration of Compound (1) on female rat **sexual** proceptivity.
FIG. 5: Inhibitory effect of NMB on female rat **sexual** proceptivity and antagonism of this effect by Compound (1).
FIG. 6: Results of an investigation to show whether the effect of Compound (1)

on female **sexual** behaviour is mediated through progesterone.
FIG. 7: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through oestradiol.
FIG. 8: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through prolactin.
FIG. 9: Results of an investigation to show whether the effect of Compound on female **sexual** behaviour is mediated through LH.
FIG. 10: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through FSH.
FIG. 11: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Mount Latency).
FIG. 12: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Intromission Latency).
FIG. 13: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Number of Mounts+Intromission).
FIG. 14: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Ejaculation Latency).
FIG. 15: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Refractory Period).
FIG. 16: Effect of Compound (1) on the **sexual** behaviour of ***sexually*** **dysfunctional** male rats (Mount Latency).
FIG. 17: Effect of Compound (1) on the **sexual** behaviour of ***sexually*** **dysfunctional** male rats (Ejaculation Latency).
FIG. 18: Effect of Compound (1) on the **sexual** behaviour of ***sexually*** **dysfunctional** male rats (% animals ejaculating).
FIG. 19: Effect of (S)-3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2ylamino)-propionamide (Compound (2)) in PEG 200 on female rat **sexual** proceptivity.
FIG. 20: Effect of Compound (2) in methylcellulose on female rat **sexual** proceptivity.
FIG. 21: Effect of Compound (2) in PEG 200 on female rat **sexual** receptivity.
FIG. 22: Effect of compound 1 on basal and pelvic nervestimulated increases in female genital blood flow in the anaesthetised rabbit model of female ***sexual*** arousal.
FIG. 23: Effect of (2S)-N-((1-(4-aminophenyl)cyclohexyl)methyl)3-(1H-indol-3-yl)-2-methyl-2-(((4-nitroanilino)carbonyl)amino) propanamide (Compound 3) on basal and pelvic nerve-stimulated increases female genital blood flow in the anaesthetised rabbit model of female **sexual** arousal.
FIG. 24: Effect of compound 1 on penile intracavemosal pressure in the conscious male rat.
FIG. 25: Effect of compound 3 on penile intracavernosal pressure in the conscious male rat model of penile erection.
FIG. 26: Effect of compound 3 alone and in combination with a phosphodiesterase type five inhibitor on basal and pelvic nervestimulated increases penile intracavernosal pressure in the anaesthetised rabbit model of penile erection.

TI TREATMENT OF **SEXUAL DYSFUNCTION**

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of **sexual dysfunction** in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compounds, for example PDE5 inhibitors, NEP inhibitors and lasofoxifene.

GI 26 Figure(s).
FIG. 1: Effect of (S) 3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)propionamide (Compound (1)) on female rat **sexual** proceptivity.

FIG. 2: Effect of Compound (1) on female rat **sexual** receptivity.
FIG. 3: Effect of repeated administration of Compound (1) on female rat proceptivity.
FIG. 4: Effect of intracerebroventricular administration of Compound (1) on female rat **sexual** proceptivity.
FIG. 5: Inhibitory effect of NMB on female rat **sexual** proceptivity and antagonism of this effect by Compound (1).
FIG. 6: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through progesterone.
FIG. 7: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through oestradiol.
FIG. 8: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through prolactin.
FIG. 9: Results of an investigation to show whether the effect of Compound on female **sexual** behaviour is mediated through LH.
FIG. 10: Results of an investigation to show whether the effect of Compound (1) on female **sexual** behaviour is mediated through FSH.
FIG. 11: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Mount Latency).
FIG. 12: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Intromission Latency).
FIG. 13: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Number of Mounts+Intromission).
FIG. 14: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Ejaculation Latency).
FIG. 15: Effect of Compound (1) on the **sexual** behaviour of normal male rats (Refractory Period).
FIG. 16: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (Mount Latency).
FIG. 17: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (Ejaculation Latency).
FIG. 18: Effect of Compound (1) on the **sexual** behaviour of **sexually dysfunctional** male rats (% animals ejaculating).
FIG. 19: Effect of (S)-3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2ylamino)-propionamide (Compound (2)) in PEG 200 on female rat **sexual** proceptivity.
FIG. 20: Effect of Compound (2) in methylcellulose on female rat **sexual** proceptivity.
FIG. 21: Effect of Compound (2) in PEG 200 on female rat **sexual** receptivity.
FIG. 22: Effect of compound 1 on basal and pelvic nervestimulated increases in female genital blood flow in the anaesthetised rabbit model of female **sexual** arousal.
FIG. 23: Effect of (2S)-N-((1-(4-aminophenyl)cyclohexyl)methyl)3-(1H-indol-3-yl)-2-methyl-2-(((4-nitroanilino)carbonyl)amino) propanamide (Compound 3) on basal and pelvic nerve-stimulated increases female genital blood flow in the anaesthetised rabbit model of female **sexual** arousal.
FIG. 24: Effect of compound 1 on penile intracavemosal pressure in the conscious male rat.
FIG. 25: Effect of. . .

ECLM D R A W I N G

DELACROIX

1. A method of treating **sexual dysfunction** which comprises administering to a subject suffering therefrom and in need of treatment an effective amount of a **bombesin** receptor antagonist.

ACLM 3. The method of claim 2, wherein the subject is suffering from **erectile dysfunction**.

4. The method of claim 3, wherein the subject is suffering from **erectile dysfunction** that is psychogenic.

5. The method of claim 3, wherein the subject is suffering from **erectile dysfunction** that is hormonal or endocrinologic.

6. The method of claim 3, wherein the subject is suffering from **erectile dysfunction** that is neurogenic.

7. The method of claim 3, wherein the subject is suffering from **erectile dysfunction** that is drug-induced.

8. The method of claim 3, wherein the subject is suffering from **erectile dysfunction** that is arteriogenic and/or venogenic and/ or related to cavernosal factors.

9. The method of claim 2, wherein the subject is suffering from hypoactive **sexual** desire.

12. The method of claim 11, wherein the subject is suffering from **sexual** arousal disorder.

13. The method of claim 12, wherein the subject is suffering from **sexual** arousal disorder that is arteriogenic and/or vasculogenic.

14. The method of claim 12, wherein the subject is suffering from **sexual** arousal disorder that is neurogenic.

15. The method of claim 12, wherein the subject is suffering from **sexual** arousal disorder that is hormonal or endocrine.

16. The method of claim 12, wherein the subject is suffering from **sexual** arousal disorder that is psychogenic.

17. The method of claim 12, wherein the subject is suffering from **sexual** arousal disorder that is drug-induced.

18. The method of claim 11, wherein the subject is suffering from hypoactive **sexual** desire disorder.

20. The method of claim 11, wherein the subject is suffering from **sexual** pain disorder.

21. The method of claim 1, wherein the **dysfunction** is associated with generalised unresponsiveness and/or ageing-related decline in **sexual** arousability.

22. The method of claim 1, wherein the **bombesin** receptor antagonist is a selective **bombesin** BB1 antagonist.

23. The method of claim 22, wherein the **bombesin** BB1 antagonist has a selectivity for BB1 over the other **bombesin** receptor subtypes greater than 10.

24. The method of claim 22, wherein the **bombesin** BB1 antagonist has a selectivity for BBI over the other **bombesin** receptor subtypes greater than 30.

25. The method of claim 22, wherein the **bombesin** BB1 antagonist has a selectivity for BB1 over the other **bombesin** receptor subtypes greater than 100.

26. The method of claim 1, wherein the **bombesin** receptor antagonist is a mixed BB1/BB2 antagonist.

27. The method of claim 1, wherein the **bombesin** receptor antagonist has a Ki against BB1 of less than 1000 nM.

28. The method of claim 1, wherein the **bombesin** receptor antagonist has a Ki against BB1 of less than 500 nM.

29. The method of claim 1, wherein the **bombesin** receptor

antagonist has a Ki against BB1 of less than 100 nM.
30. The method of claim 1, wherein the **bombesin** receptor antagonist has a Ki against BB1 of less than 50 nM.
31. The method of claim 1, wherein the **bombesin** receptor antagonist has a Ki against BB1 of less than 10 nM.
32. The method of claim 1, wherein there is administered to the subject an effective amount of a non-peptide **bombesin** receptor antagonist.
33. The method of claim 32, wherein the non-peptide **bombesin** receptor antagonist is a compound that is absorbable when administered orally.
34. The method of claim 1, wherein there is administered to the subject an effective amount of a **bombesin** receptor antagonist which is a peptide.
35. A method of treating **sexual dysfunction** in a male or female subject suffering therefrom and in need of treatment which comprises administering to the subject an effective amount of a **bombesin** receptor antagonist and a PDE 5 inhibitor.
36. A method of treating **sexual dysfunction** in a male or female subject suffering therefrom and in need of treatment which comprises administering to the subject an effective amount of a **bombesin** receptor antagonist and a NEP inhibitor.
37. A method of treating **sexual dysfunction** in a female subject suffering therefrom and in need of treatment which comprises administering to the subject an effective amount of a **bombesin** receptor antagonist and one or more estrogen receptor modulators (SERM) and/or estrogen agonists and/or estrogen antagonists.
38. A method of treating **sexual dysfunction** in a male or female subject suffering therefrom and in need of treatment which comprises administering to the subject an effective amount of a **bombesin** receptor antagonist and lasofoxifene.
39. A pharmaceutical combination (for simultaneous, separate or sequential administration) of a **bombesin** receptor antagonist and one or more materials selected from (1) to (34) below: (1) naturally occurring or synthetic prostaglandins or. . . agonists or modulators for oxytocin/vasopressin receptors; and (34) modulators of cannabinoid receptors. 40 The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound of the formula (I)

D R A W I N G

or a pharmaceutically acceptable. . .
41. The combination of claim 39, wherein the **bombesin** receptor antagonist is a compoundof Formula (Ia)

D R A W I N G

wherein Ar is phenyl unsubstituted or. . .
42. The combination of claim 40, wherein the **bombesin** receptor antagonist is a compound of Formula I wherein Ar is unsubstituted phenyl; R1 is cyclopentyl or tert-butyl; R4 and. . .
43. The combination of claim 40, wherein the **bombesin** receptor antagonist is a compound of Formula I wherein Ar is 2,6-diisopropyl-phenyl, 4-nitro-phenyl, and 4-cyano-phenyl; R4, R5, and R6 are. . .
44. The combination of claim 39, wherein the **bombesin** receptor antagonist is (S)3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl) -cyclohexylmethyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)-propionamide (also referred to as Compound 1) or one of its pharmaceutically acceptable salts or is. . .
45. The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound set out below or a pharmaceutically acceptable

salt thereof: (S) N-cyclohexylmethyl-2-(3-(2,6-diisopropyl-phenyl)-ureido)-3-(1H-indol-3-yl)-2-methyl-propionamide; N-cyclohexylmethyl-2-(3-(2,6-diisopropyl-phenyl)-ureido)-3-(1H-indol-3-yl)-N-methyl-propionamide; N-cyclohexylmethyl-2-(3-(2,6-diisopropyl-phenyl)-1-methyl-ureido)-3-(1H-indol-3-yl)-propionamide; 2-(3-(2,6-diisopropyl-phenyl)-ureido)-2-methyl-3-(1-oxy-pyridin-2-yl)-N-(1. . .

46. The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound of formula (II) or a pharmaceutically acceptable salt thereof:

D R A W I N. . . to 7 carbon atoms, containing up to 2 oxygen or nitrogen atoms. 47 The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound of the formula (IIa), or a pharmaceutically acceptable salt thereof:

D R A W I. . .

48. The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound has the formula (IIb) or (IIc) or is a pharmaceutically acceptable salt thereof:

D R. . .

49. The combination of claim 39, wherein the **bombesin** receptor antagonist is (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-propionamide (also referred to as Compound 2) or a pharmaceutically acceptable salt. 50 The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a pharmaceutically acceptable salt thereof: (S)-3-(1H-indol-3-yl)-N-(1-methoxymethyl-cyclohexylmethyl)-2-methyl-2-(4-(4 -nitro-phenyl)-oxazol-2-ylamino)-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-N-(2 -oxo-2-phenyl-ethyl)-propionamide; (S)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro -phenyl)-oxazol-2-ylamino)-3-phenyl-propionamide;. . . (S)-2-(biphenyl-2-ylamino)-3-(1H-indol-3-yl)-2-methyl-N-(1-pyridin-2-yl -cyclohexylmethyl)-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-N-(1-pyridin-2-yl-cyclohexylmethyl)-2-m -tolylamino-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-2-(6-phenyl-pyridin-2-ylamino)-N-(1-pyridin-2-yl-cyclohexylmethyl)-propionamide; (R)-3-phenyl-2-phenylamino-N-(1-pyridin-2-yl-cyclohexylmethyl)-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-2-phenylethylamino-N-(1-pyridin-2-yl-cyclohexylmethyl)-propionamide; (S)-2-((benzofuran-2-ylmethyl)-amino)-3-(1H-indol-3-yl)-2-methyl-N-(1 -pyridin-2-yl-cyclohexylmethyl)-propionamide, and (S)-3-(1H-indol-3-yl)-2-methyl-2-(4-nitro-benzylamino)-N-(1-pyridin-2-yl -cyclohexylmethyl)-propionamide. 51 The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound of formula (III) or a pharmaceutically acceptable salt thereof:

D R A W I N. . .

52. The combination of claim 51, wherein the **bombesin** receptor antagonist is a compound formula (III) in which: k is 0 or 1; l is 1; m is 0. . .

53. The combination of claim 51, wherein the **bombesin** receptor antagonist is a compound of Formula (III) in which, l is 1; m is 1; n is 0; R2. . .

54. The combination of claim 39, wherein the **bombesin** receptor antagonist is a compound of formula (IIIa) or a salt thereof:

D R A W I N G

wherein. . .

55. The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof: N-((S)-2-(1H-indol-3-yl)-1-methyl-I -((1-pyridin-2-yl-cyclohexylmethyl)-

carbamoyl)-ethyl)-4-nitro-benzamide; C-dimethylamino-N-((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl -cyclohexylmethyl)-carbamoyl)-ethyl)-benzamide; 1H-indole-2-carboxylic acid ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-amide;. . .

56. The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof N-((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-benzamide; N-((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-4-methyl-benzamide; 4-chloro-N-((S)-2-(iH-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl -cyclohexylmethyl)-carbamoyl)-ethyl)-benzamide; N-((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-4-methoxy-benzamide;. . .

57. The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-carbamic acid naphthalen-1-ylmethyl ester; ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-carbamic acid. . .

58. The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof: ((S)-2-(1H-indol-3-yl)-1-methyl-I -((1-pyridin-2-yl-cyclohexylmethyl)-carbamoyl)-ethyl)-carbamic acid 3,4-dimethoxy-benzyl ester; ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-carbamic acid. . . ester; ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-carbamic acid 3-phenoxy-benzyl ester; and ((S)-2-(1H-indol-3-yl)-1-methyl-1-((1-pyridin-2-yl-cyclohexylmethyl) -carbamoyl)-ethyl)-carbamic acid 4-methyl-benzyl ester. 59 The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof: (S)-3-(1H-indol-3-yl)-2-methyl-2-phenylmethanesulfonylamino-N-(1-pyridin-2 -yl-cyclohexylmethyl)-propionamide; (S)-2-(2-chloro-benzenesulfonylamino)-3-(1H-indol-3-yl)-2-methyl-N-(1 -pyridin-2-yl-cyclohexylmethyl)-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-2-(naphthalene-1-sulfonylamino)-N-(1-pyridin -2-yl-cyclohexylmethyl)-propionamide; (S)-3-(1H-indol-3-yl)-2-methyl-N-(1-pyridin-2-yl-cyclohexylmethyl)-2 -(quinoline-8-sulfonylamino)-propionamide;. . .

60. The combination of claim 39, wherein the **bombesin** receptor antagonist is one of the following compounds or a salt thereof: (S)-3-(1H-indol-3-yl)-2-methyl-N-(1-pyridin-2-yl-cyclohexylmethyl)-2 -(toluene-4-sulfonylamino)-propionamide; (S)-3-(1H-indol-3-yl)-2-methanesulfonylamino-2-methyl-N-(1-pyridin-2-yl -cyclohexylmethyl)-propionamide; (S)-2-(2-fluoro-benzenesulfonylamino)-3-(1H-indol-3-yl)-2-methyl-N-(1 -pyridin-2-yl-cyclohexylmethyl)-propionamide; (S)-2-(4-chloro-benzenesulfonylamino)-3-(1H-indol-3-yl)-2-methyl-N-(1 -pyridin-2-yl-cyclohexylmethyl)-propionamide;. . .

. . . a combination as claimed in claim 39 in the preparation of a medicament for the treatment or prophylaxis of male **sexual dysfunction** (more particularly male **erectile dysfunction**) and/or female **sexual dysfunction** (more particularly hypoactive **sexual** desire disorders, **sexual** arousal disorders, anorgasmic disorders or **sexual** pain disorders.

64. A pharmaceutical combination (for simultaneous, separate or sequential administration) of a **bombesin** receptor antagonist and a PDE 5 inhibitor.

65. A pharmaceutical combination (for simultaneous, separate or sequential administration) of a **bombesin** receptor antagonist and a NEP inhibitor.
66. A pharmaceutical combination (for simultaneous, separate or sequential administration) of a **bombesin** receptor antagonist and one or more estrogen receptor modulators (SERM) and/or estrogen agonists and/or estrogen antagonists.
67. A pharmaceutical combination (for simultaneous, separate or sequential administration) of a **bombesin** receptor antagonist and lasofoxifene.

L7 ANSWER 16 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-706891 [76] WPIDS
AB WO 200260923 A UPAB: 20021125
NOVELTY - Isolated peptides selected from amino acid sequences (as given in the specification), their analogues and derivatives are new.

DETAILED DESCRIPTION - Isolated peptides selected from amino acid sequences, their analogues and derivatives are new. The amino acid sequences are 179 sequence's as given in the specification e.g. His-Asp-His-Gly-Ile-Arg-Xaa3-Lys-Arg-Val-Asp-Ile-Cys-Asn-Xaa4-Arg-Ile-Cys-Ala-Xaa3-Asn-Xaa3-Leu-Arg- Arg-His-Asp-Leu-Lys-Lys-Gly-Asn-Asn- and Xaa2-ser-Gly-Cys-Arg-val-Xaa3-Phe-Xaa1-Leu-Lys-Cys-Ile-Xaa4-Lys-Phe-Cys-Thr-Ile- Xaa5-Xaa3-Ser-Arg-Xaa3-Phe-Ala-Ser-Leu-Xaa1-Xaa1-Lys-Asp-Xaa1-Cys-Gln-Thr-Val-Thr-Ile-Thr-Val-Thr-Xaa4-Asp-Phe-.

Xaa1 = gamma -carboxy-Glu;
Xaa2 = Gln or pyro-Glu;
Xaa3 = Pro or trans-4-hydroxy-Pro;
Xaa4 = D or L Trp or D or L 6 bromo-Trp;
Xaa5 = Tyr, mono-iodo-Tyr, 125I-Tyr, di-iodo-Tyr, O-silpho-Tyr or O-phospho-Tyr.

INDEPENDENT CLAIMS are also included for the following:

(1) An isolated nucleic acid encoding a beta -superfamily conopeptide propeptide. The propeptide is selected from 75 amino acid sequences as given in the specification e.g. Met-Gln-Thr-Ala-Tyr-Trp-Val-Met-Met-Val-Trp-Ile-Thr-Ala-Pro-Leu-Ser-Glu-Gly-Lys-Leu-Asn-Asp-Val-Trp-Ile-Arg-Gly-Leu-Val-Pro-Asp-Asp-Leu-Thr-Pro-Gln-Leu-Ile-Leu-Gln-Ser-Leu-Asp-Ser-Arg-Arg-His-Gly-Ile-Arg-Pro-Lys-Arg-Val-Asp-Ser-Arg-Arg-His-Asp-His-Gly-Ile-Arg-Pro-Lys-Arg-Val-Asp-Ile-Cys-Asn-Trp-Arg-Ile-Cys-Ala-Pro-Asn-Pro-Leu-Arg-His-Asp-Leu-Lys-Lys-Gly-Asn-Asn;

(2) Treatment of cancer involves administering a peptide (preferably beta -superfamily conotoxin) tagged with a radionuclide;

(3) Treatment or prevention of disorders associated with a disorder selected from voltage-gated ion channel disorders, ligand-gated ion channel disorder and receptor disorder such as disorders of G-protein coupled receptors (GPCR);

(4) Identifying drug candidates by administering a beta -superfamily conotoxin involving: screening a drug candidate for its action at or partially at the same functional site as a beta -superfamily conotoxin and capable of elucidation of similar functional response as the conotoxin;

(5) Identifying compounds that mimic the therapeutic activity of the beta -superfamily conotoxin involving conducting a biological assay on a test compound to determine the therapeutic activity and comparing the results to the results obtained from the biological assay of beta -superfamily conotoxin;

(6) Identifying a ligand which binds to an orphan G-protein coupled receptor (orphan GPCR) involving contacting a peptide or a radiolabeled derivatives of the peptide with an orphan GPCR and measuring the amount of

binding of the peptide to the orphan GPCR; and

(7) Designing a beta - beta turn mimetic of a beta -superfamily conotoxin comprising a beta -turn motif by replacing this motif with a non-peptide turn mimetic beta -turn scaffold and then attaching receptor binding domains contained within the N and C-terminal sequences of a beta -superfamily conotoxin to the beta -turn scaffold to mimic the 3D spatial array within the native beta -superfamily conotoxin. The beta -turn motif is selected from -CX1X2KX1C- (SEQ ID NO:338) motif or -CPX3RVC- (SEQ ID NO:339) motif.

X1 = amino acid;

X2 = D or L Trp or D or L 6-bromo Trp;

X3 = D or L Phe.

ACTIVITY - Vasotropic; Anorectic; antiinflammatory; Cytostatic; Antitumor; Antidiabetic; Nephrotropic; Gastrointestinal-Gen.; Antidiarrheic; Ophthalmological; Analgesic; Antidepressant; Cardiant; Cerebroprotective; Anticonvulsant; Neuroleptic; Osteopathic; Antianginal; Antiseborrheic; Dermatological;

MECHANISM OF ACTION - G-protein-coupled receptor (GPCR) allosteric modulator.

USE - For treating or preventing disorders associated with a disorder selected from voltage-gated ion channel disorders, ligand-gated ion channel disorder and receptor disorder such as disorders of G-protein coupled receptors e.g. disorder associated with a melanocortin system or MCR **dysfunction** (such as **erectile dysfunction**, obesity inflammation, melanoma), cancer neoplasm, solid tumor, diabetic nephropathy, fibrosis, hypophysis tumor, GI disease, irritable bowel syndrome, restenosis, angiogenesis disorder, diabetic mellitus, endocrine tumor, diarrhea, pancreatic disease, prostate tumor, bleeding, apoptosis, inflammation, pain (e.g. visceral pain), **sexual dysfunction**, acromegaly, glaucoma, cardiovascular, diabetic retinopathy, depression, myocardial infarction, stroke, epilepsy, anorexia, wasting disease, seborrheic dermatitis, schizophrenia, mood disorder, chemotherapeutic induced emesis, disorder associated with changes in blood pressure, immune disorder, nerve damage, acne, GI infections, angina, thromboembolism, cardiovascular disease and osteoporosis (claimed)

ADVANTAGE - The peptide has activity at somatostatin receptors or melanocortin receptor.

Dwg.0/0

ACCESSION NUMBER: 2002-706891 [76] WPIDS
DOC. NO. CPI: C2002-200471
TITLE: New beta-superfamily conotoxin peptides useful for treating e.g. cancer, **erectile dysfunction**, obesity inflammation, diabetic nephropathy, fibrosis, irritable bowel syndrome, restenosis, angiogenesis disorder.
DERWENT CLASS: B04 D16 K08
INVENTOR(S): GARRETT, J E; JONES, R M; OLIVERA, B M; WATKINS, M
PATENT ASSIGNEE(S): (COGN-N) COGNETIX INC; (UTAH) UNIV UTAH RES FOUND
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002060923	A2	20020808	(200276)*	EN	230

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003170222 A1 20030911 (200367)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002060923 A2		WO 2002-US2523	20020129
US 2003170222 A1	Provisional	US 2001-264323P	20010129
		US 2002-58053	20020129

PRIORITY APPLN. INFO: US 2001-264323P 20010129; US 2002-58053 20020129

TI New beta-superfamily conotoxin peptides useful for treating e.g. cancer, **erectile dysfunction**, obesity inflammation, diabetic nephropathy, fibrosis, irritable bowel syndrome, restenosis, angiogenesis disorder.

AB . . .
disorder and receptor disorder such as disorders of G-protein coupled receptors e.g. disorder associated with a melanocortin system or MCR **dysfunction** (such as **erectile dysfunction**, obesity inflammation, melanoma), cancer neoplasm, solid tumor, diabetic nephropathy, fibrosis, hypophysis tumor, GI disease, irritable bowel syndrome, restenosis, angiogenesis disorder, diabetic mellitus, endocrine tumor, diarrhea, pancreatic disease, prostate tumor, bleeding, apoptosis, inflammation, pain (e.g. visceral pain), **sexual dysfunction**, acromegaly, glaucoma, cardiovascular, diabetic retinopathy, depression, myocardial infarction, stroke, epilepsy, anorexia, wasting disease, seborrheic dermatitis, schizophrenia, mood disorder, chemotherapeutic induced. . .

TECH. . .
orexin, urotensin, glycoprotein IIB/IIIa, thrombin receptor or orphan GPCR. The GPCR is MCH2R/SLT, SP1999/P2Y12, CRTH2, NPFF1, NPFF2, HH4R, h-GPR54, CysLT2, **neuromedin** receptor, BLTR2, G2A, TA1, LTB4, ghrelin, motilin MTL-R, purinergic receptor, muscarinic receptor, ORL-1, apelin, CB1, CB2 or GPCR of orphan. . .

L7 ANSWER 17 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-547828 [58] WPIDS
CR 2002-155042 [20]; 2002-179661 [23]; 2002-241363 [29]; 2002-740638 [80]
AB WO 200247670 A UPAB: 20031216
NOVELTY - Use of an inhibitor (NPYi) of a neuropeptide Y (NPY) for the treatment or prevention of male **erectile dysfunction** (MED).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) Use a neuropeptide Y Y1 receptor (NP Y1) inhibitor (NP Y1i) for the treatment or prevention of male **erectile dysfunction** (MED);

(2) An assay method (M1) for identifying an agent that can be used to treat to MED comprising:

(a) determining whether the test agent (A) (such as NPYi) directly enhances the endogenous **erectile** process;

(3) A process (M2) involving:

(a) performing (M1);

(b) identifying at least one agent capable of inhibiting NPY or NPY Y1; and

(c) preparing a quantity of those identified agents (NPYi or NPY Y1i);

(4) An assay method (M3) comprising:

(a) contacting (A) which has a moiety capable of inhibiting the metabolic breakdown of a peptide (preferably a fluorescent labeled peptide); and

(b) measuring the activity and/or levels of peptide remaining after a fixed time (e.g. via fluorometric analysis. Where the change in the level of the peptide measured by fluorescence is indicative of the potency of (A);

(5) A diagnostic method (M4) involves:

(a) isolating a sample from a male; and

(b) determining whether the sample contains an entity present in such an amount as to cause MED and has a direct effect on the endogenous **erectile** process in the corpus cavernosum of the male;

(6) A diagnostic composition or kit comprising (A);

(7) An animal model for identifying an agent capable of treating MED comprising:

(a) an anaesthetized animal; and

(b) the means to measure changes in intracavernosal pressure and/or cavernosal blood flow of animal following stimulation of the pelvic nerve;

(8) An assay method (M5) involves administering an agent to the animal model and measuring the change in the endogenous **erectile** process; and

(9) A combination containing at least one NPYi and at least one auxiliary active agents (e.g. PDE inhibitor) in the manufacture/preparation of a medicament for the treatment or prevention of MED.

ACTIVITY - Vasotropic; Anorectic.

Submaximal increases in intracavernosal pressure (ICP) induced by nerve stimulation were significantly increased in the presence of increasing doses of ((2-diphenylacetylamino-5-guanidino-pentanoyl)-4-hydroxy-benzylamide), a selective NPY Y1 receptor antagonist.

The increase became significant at doses at least 30 micro g/kg. The maximum potentiation (approximately 127%) was observed at 30 micro g/kg.

MECHANISM OF ACTION - Neuropeptide Y (NPY) inhibitor; NPY receptor antagonist.

USE - For treatment or prevention of male **erectile dysfunction**, abnormal drink and food intake disorders (e.g. obesity, anorexia, bulimia or metabolic disorders) (claimed).

ADVANTAGE - The inhibitor has no activity towards endopeptidase (NEP) and/or angiotensin converting enzyme; selectively increases intracavernosal pressure of the penis which facilitates and/or causes penile erection during **sexual** arousal; is highly selective for NPY/NPY Y1 located in male genitalia and for NPY and/or NPY Y1 receptors associated with the corpus cavernosum. The NPY inhibitors enhance the nerve-stimulated **erectile** process and are highly selective for reproductive tract to overcome an **erectile dysfunction** without the risk of adverse side effects, particularly a drop in blood pressure.

Dwg.0/10

ACCESSION NUMBER: 2002-547828 [58] WPIDS

CROSS REFERENCE: 2002-155042 [20]; 2002-179661 [23]; 2002-241363 [29]; 2002-740638 [80]

DOC. NO. CPI: C2002-155371
TITLE: Use of an inhibitor of neuropeptide Y in the preparation of medicament for the treatment or prevention of male **erectile dysfunction**.
DERWENT CLASS: B04
INVENTOR(S): BENSON, N; BOYD, H F; CONTILLO, L G; SINGLETON, D H; STACEY, P; GONZALEZ, M I; HIGGINBOTTOM, M; NAYLOR, A M; PINNOCK, R D; PRITCHARD, M C; STOCK, H T; VAN DER GRAAF, P H; WAYMAN, C P
PATENT ASSIGNEE(S): (NAYL-I) NAYLOR A M; (GONZ-I) GONZALEZ M I; (HIGG-I) HIGGINBOTTOM M; (PINN-I) PINNOCK R D; (PRIT-I) PRITCHARD M C; (STOC-I) STOCK H T; (VGRA-I) VAN DER GRAAF P H; (WAYM-I) WAYMAN C P; (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002047670	A1	20020620	(200258)*	EN	179
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002020977	A	20020624	(200267)		
US 2002169101	A1	20021114	(200277)		
EP 1275733	A2	20030115	(200306)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
CA 2393376	A1	20030113	(200313)	EN	
JP 2003135064	A	20030513	(200340)		92
US 2003119714	A1	20030626	(200343)		
EP 1347750	A1	20031001	(200365)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
KR 2003061441	A	20030718	(200381)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002047670	A1		WO 2001-IB2399	20011210
AU 2002020977	A		AU 2002-20977	20011210
US 2002169101	A1	Provisional	US 1999-133355P	19990510
		CIP of	WO 2000-GB1787	20000510
		CIP of	US 2000-700165	20001109
		CIP of	US 2001-759777	20010112
			US 2001-999284	20011115
EP 1275733	A2		EP 2002-254616	20020701
CA 2393376	A1		CA 2002-2393376	20020711
JP 2003135064	A		JP 2002-205433	20020715
US 2003119714	A1	Provisional	US 2001-265358P	20010131
		Provisional	US 2001-291722P	20010517
		CIP of	US 2001-895367	20010629
		CIP of	US 2001-905846	20010713
			US 2001-17273	20011212

EP 1347750	A1	EP 2001-270206	20011210
		WO 2001-IB2399	20011210
KR 2003061441 A		KR 2003-707946	20030613

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002020977 A		Based on	WO 2002047670
EP 1347750	A1	Based on	WO 2002047670

PRIORITY APPLN. INFO: GB 2001-20679 20010824; GB 2000-30647 20001215; GB 2001-8730 20010406; GB 2001-9910 20010423; GB 2001-11037 20010504; US 2001-895367 20010629; US 2001-905846 20010713; US 2001-948429 20010907

TI Use of an inhibitor of neuropeptide Y in the preparation of medicament for the treatment or prevention of male **erectile dysfunction**
.

AB . . . 20031216
NOVELTY - Use of an inhibitor (NPYi) of a neuropeptide Y (NPY) for the treatment or prevention of male **erectile dysfunction** (MED).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) Use a neuropeptide Y Y1 receptor (NP Y1) inhibitor (NP Y1i) for the treatment or prevention of male **erectile dysfunction** (MED);
(2) An assay method (M1) for identifying an agent that can be used to treat to MED comprising:
(a) determining whether the test agent (A) (such as NPYi) directly enhances the endogenous **erectile** process;
(3) A process (M2) involving:
(a) performing (M1);
(b) identifying at least one agent capable of inhibiting NPY or. . . contains an entity present in such an amount as to cause MED and has a direct effect on the endogenous **erectile** process in the corpus cavernosum of the male;
(6) A diagnostic composition or kit comprising (A);
(7) An animal model. . . (8) An assay method (M5) involves administering an agent to the animal model and measuring the change in the endogenous **erectile** process; and
(9) A combination containing at least one NPYi and at least one auxiliary active agents (e.g. PDE inhibitor). . . MECHANISM OF ACTION - Neuropeptide Y (NPY) inhibitor; NPY receptor antagonist.
USE - For treatment or prevention of male **erectile dysfunction**, abnormal drink and food intake disorders (e.g. obesity, anorexia, bulimia or metabolic disorders) (claimed).
ADVANTAGE - The inhibitor has. . . endopeptidase (NEP) and/or angiotensin converting enzyme; selectively increases intracavernosal pressure of the penis which facilitates and/or causes penile erection during **sexual** arousal; is highly selective for NPY/NPY Y1 located in male genitalia and for NPY and/or NPY Y1 receptors associated with the corpus cavernosum. The NPY inhibitors enhance the nerve-stimulated **erectile** process and are highly selective for reproductive tract to overcome an **erectile dysfunction** without the risk of adverse side effects, particularly a drop in blood pressure.

Dwg.0/10
TECH. . .
neurokinin (NK) receptor antagonist;
(xxxii) opioid receptor agonist, antagonist or modulator;
(xxxiii) agonist or modulator for oxytocin/vasopressin receptors;
(xxxiv) modulators of cannabinoid receptors;
(xxxv) **bombesin** receptor antagonist;
(xxxvi) an secreted endopeptidase (SEP) inhibitor;
(xxxvii) an agent capable of modulating the activity of an intermediate conductance calcium-activated potassium. . .

L7 ANSWER 18 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-740638 [80] WPIDS
CR 2002-155042 [20]; 2002-179661 [23]; 2002-454833 [48]; 2002-489427 [52]; 2002-547828 [58]
AB WO 200240008 A UPAB: 20040120
NOVELTY - Pharmaceutical combination comprises **bombesin** receptor antagonists and at least one vasodilator, hormone therapy or neurotransmitter modulator.
DETAILED DESCRIPTION - Pharmaceutical combination (A) comprises **bombesin** receptor antagonists (B) and at least one material selected from:
(1) naturally occurring or synthetic prostaglandins or their esters;
(2) alpha -adrenergic receptor antagonist compounds also known as a adrenoceptor antagonists or alpha -receptor antagonists or alpha -blockers;
(3) NO-donor (NO-agonist) compounds;
(4) potassium channel openers or modulators;
(5) dopaminergic agents;
(6) vasodilator agents;
(7) thromboxane A2 agonists;
(8) central nervous system (CNS) active agents;
(9) ergot alkaloids;
(10) compounds which modulate the action of natriuretic factors;
(11) angiotensin receptor antagonists such as losartan;
(12) substrates for NO-synthase;
(13) calcium channel blockers;
(14) cholesterol lowering agents;
(15) antiplatelet and antithrombotic agents;
(16) insulin sensitizing agents and hypoglycemic agents;
(17) L-DOPA or carbidopa;
(18) acetylcholinesterase inhibitors;
(19) steroidal or non-steroidal anti-inflammatory agents;
(20) estrogen receptor modulators and/or estrogen agonists and/or estrogen antagonists and their salts;
(21) PDE inhibitors;
(22) neuropeptide Y (NPY) inhibitors;
(23) NEP inhibitors;
(24) vasoactive intestinal proteins (VIP), VIP mimetics, VIP analogues, VIP receptor agonists or VIP analogues or VIP fragments, or alpha -adrenoceptor antagonists with VIP combinations;
(25) melanocortin receptor agonists or modulators or melanocortin enhancers;
(26) serotonin receptor agonists, antagonists or modulators;
(27) testosterone replacement agents, testosterone, dihydrotestosterone or a testosterone implant;
(28) estrogen, estrogen and medroxyprogesterone or

medroxyprogesterone acetate (MPA) (i.e. as a combination), or estrogen and methyl testosterone hormone replacement therapy agents;

(29) modulators of transporters for noradrenaline, dopamine and/or serotonin;

(30) purinergic receptor agonists and/or modulators;

(31) neurokinin (NK) receptor antagonists;

(32) opioid receptor agonists, antagonists or modulators;

(33) agonists or modulators for oxytocin/vasopressin receptors; or

(34) modulators of cannabinoid receptors.

An INDEPENDENT CLAIM is included for use of (A) in the preparation of medicament.

ACTIVITY - Vasotropic; Analgesic; Cardiovascular; Antiarteriosclerotic; Antilipemic; Antismoking; Antidiabetic; Hypotensive; Tranquilizer; Vulnerary; central nervous system; Neuroprotective; Antiparkinsonian; Cerebroprotective; Antiinflammatory; Antidepressant.

MECHANISM OF ACTION - Bombesin (BB) receptor antagonist; BB receptor binder.

USE - For the treatment or prophylaxis of male sexual dysfunction (preferably male erectile dysfunction (MED)) and/or female sexual dysfunction (FSD), preferably hypoactive sexual desire disorders, sexual arousal disorders, anorgasmic disorders or sexual pain disorders (claimed). Also treated are MED and FSD arising from arteriogenic/vasculogenic etiologies (e.g. cardiovascular or atherosclerotic diseases, hypercholesterolemia, cigarette smoking, diabetes, hypertension, radiation and perineal trauma and traumatic injury to the iliohypogastric pudendal vascular system), neurogenic etiologies (e.g. spinal cord injuries or diseases of the central nervous system including multiple sclerosis, Parkinsonism, cerebrovascular accidents, peripheral neuropathies, trauma and radical pelvic surgery), hormonal/endocrine etiologies (e.g. dysfunction of hypothalamic/pituitary/gonadal axis, dysfunction of the pancreas, surgical or medical castration, androgen deficiency, high circulating levels of prolactin e.g. hyperprolactinemia, hyper and hypothyroidism), psychogenic etiologies (e.g. depression, obsessive-compulsive disorder, anxiety disorder, emotional and relation issues, performance anxiety, marital discord, dysfunctional attitudes, sexual phobias, religious inhibition or traumatic past experiences), drug-induced sexual dysfunction resulting from therapy with serotonin reuptake inhibitors (SSRIs) and other antidepressant therapies (tricyclics and major tranquilizers), anti-hypertensive therapies and sympatholytic drugs.

Ovariectomized adult female Sprague Dawley rats (180-200 g) were housed in groups of 6 in a reversed lighting system for 12 hours light:dark and were then used for sexual activity tests after 2 weeks. Two stimuli animals:an intact sexually experienced male and a receptive female (ovariectomized, primed with estradiol benzoate (5 micro g) dissolved in corn oil and injected subcutaneously 48 hours before the test and with progesterone (0.5 mg) 4 hours before the test) were kept in 2 cages opposite to each other. A bombesin receptor antagonist e.g. (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexyl-methyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)-propionamide (A) dissolved in 100% beta -cyclodextrin and then diluted with saline to a final solution of 50% 2-hydroxypropyl- beta -cyclodextrin was administered intraperitoneally at doses of 3 and 10 mg/kg, in a dosing volume of 1 ml/kg, 1 hour before the tests. (A) increased the percentage of time spent investigating the male stimulus, with a male erectile dysfunction (MED) of 10 mg/kg.

ADVANTAGE - (B) is a selective bombesin BB1 antagonist and has a selectivity for BB1 over the other bombesin receptor subtypes greater than

10 (preferably greater than 30, especially greater than 100). The bombesin receptor antagonist is a mixed BB1/BB2 antagonist having Ki against BB1 less than 1000 (preferably less than 500, more preferably less than 100, most preferably less than 50, especially less than 10) nM. The non-peptide bombesin receptor antagonist is absorbable when administered orally.
Dwg.0/25

ACCESSION NUMBER: 2002-740638 [80] WPIDS
CROSS REFERENCE: 2002-155042 [20]; 2002-179661 [23]; 2002-454833 [48]; 2002-489427 [52]; 2002-547828 [58]
DOC. NO. CPI: C2002-209615
TITLE: Use of **bombesin** receptor antagonists combination with at least one vasodilator, hormone therapy or neurotransmitter modulator in the treatment of **sexual dysfunction**.
DERWENT CLASS: B05
INVENTOR(S): GONZALEZ, M I; HIGGINBOTTOM, M; NAYLOR, A M; PINNOCK, R D; PRITCHARD, M C; STOCK, H T; VAN DER GRAAF, P H; WAYMAN, C P
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO; (WARN) WARNER LAMBERT CO LLC
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002040008	A2	20020523	(200280)*	EN	225
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002023802	A	20020527	(200280)		
EP 1333824	A2	20030813	(200355)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001015364	A	20030923	(200373)		
KR 2003051843	A	20030625	(200373)		
HU 2003001892	A2	20031128	(200405)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002040008	A2	WO 2001-GB5018	20011114
AU 2002023802	A	AU 2002-23802	20011114
EP 1333824	A2	EP 2001-994552	20011114
		WO 2001-GB5018	20011114
BR 2001015364	A	BR 2001-15364	20011114
		WO 2001-GB5018	20011114
KR 2003051843	A	KR 2003-706713	20030516
HU 2003001892	A2	WO 2001-GB5018	20011114
		HU 2003-1892	20011114

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2002023802 A Based on WO 2002040008
EP 1333824 A2 Based on WO 2002040008
BR 2001015364 A Based on WO 2002040008
HU 2003001892 A2 Based on WO 2002040008

PRIORITY APPLN. INFO: GB 2001-11037 20010504; WO 2000-GB4380 20001117; GB 2001-9910 20010423

TI Use of **bombesin** receptor antagonists combination with at least one vasodilator, hormone therapy or neurotransmitter modulator in the treatment of **sexual dysfunction**.

AB WO 200240008 UPAB: 20040120
NOVELTY - Pharmaceutical combination comprises **bombesin** receptor antagonists and at least one vasodilator, hormone therapy or neurotransmitter modulator.
DETAILED DESCRIPTION - Pharmaceutical combination (A) comprises **bombesin** receptor antagonists (B) and at least one material selected from:
(1) naturally occurring or synthetic prostaglandins or their esters;
(2). . .

TT TT: **BOMBESIN** RECEPTOR ANTAGONIST COMBINATION ONE VASODILATING HORMONE THERAPEUTIC MODULATE TREAT SEX DYSFUNCTION.

L7 ANSWER 19 OF 25 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2002:130644 TOXCENTER
CP Copyright 2004 ACS
AB This invention discloses the preparation of title compds. Ar-(CH2)k-X-NR3-CR5(CH2Ar1)-CO-NR4-(CH2)l-(CR1R6)m-(CH2)n-R2 (I) and their pharmaceutically acceptable salts as **bombesin** receptor antagonists [wherein: k = 0, 1, 2; l = 0, 1, 2, 3; m = 0, 1; n = 0, 1, 2; X = CO, OCO, SO, SO2; Ar = (un)substituted benzimidazolyl, benzofuryl, indanyl, indolyl, naphthyl, Ph, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl, thiazolyl, etc.; Ar1 = groups given for Ar, plus pyridyl N-oxide; R1 = H, alkyl, (oxa- or aza)cycloalkyl; R2 = groups given for Ar, H, OH, alkoxy, NMe2, CONR12R13, certain substituted rings; R3-R5 = H, alkyl; R6 = H, Me, or together with R1 forms carbonyl or a C3-7 ring which can contain an oxygen or nitrogen atom; provided that when X = OCO, then l = 1-3 and m = 1]. Approx. 140 specific examples of I were prepared and/or claimed. For example, HBTU-mediated coupling of 1H-indole-2-carboxylic acid with the corresponding intermediate amine provided the claimed α-methyltryptophan amide II in 60% yield. In binding studies to cloned human BB1 and BB2 **bombesin** receptor subtypes, compound II had IC50 values of 11 nM and 119 nM, resp.

DOCUMENT NUMBER: CA13626402022H
TITLE: Preparation of (S)-α-methyltryptophan amide derivatives as **bombesin** receptor antagonists
AUTHOR(S): Higginbottom, Michael; Pritchard, Martin Clive; Stock, Herman Thijs
CORPORATE SOURCE: ASSIGNEE: Warner-Lambert Company
PATENT INFORMATION: WO 2002040469 A1 23 May 2002
SOURCE: (2002) PCT Int. Appl., 85 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:391703
LANGUAGE: English
ENTRY DATE: Entered STN: 20020612

Last Updated on STN: 20030624

TI Preparation of (S)-α-methyltryptophan amide derivatives as **bombesin** receptor antagonists

AB This invention discloses the preparation of title compds. Ar-(CH2)k-X-NR3-CR5(CH2Ar1)-CO-NR4-(CH2)l-(CR1R6)m-(CH2)n-R2 (I) and their pharmaceutically acceptable salts as **bombesin** receptor antagonists [wherein: k = 0, 1, 2; l = 0, 1, 2, 3; m = 0, 1; n =. . . intermediate amine provided the claimed α-methyltryptophan amide II in 60% yield. In binding studies to cloned human BB1 and BB2 **bombesin** receptor subtypes, compound II had IC50 values of 11 nM and 119 nM, resp.

ST Miscellaneous Descriptors
bombesin receptor antagonist peptide analog methyltryptophan deriv prepn; **sexual dysfunction** treatment
bombesin receptor antagonist tryptophan methyl prepn

RN 80043-53-4 (**Gastrin-releasing peptide**)
102577-19-5 (**Neuromedin**-b)
428876-73-7 ((S)-2-((Benzo[c]-1,2,5-thiadiazol-4-ylsulfonyl)amino)-3-(1H-indol-3-yl)-2-methyl-N-((1-(pyridin-2-yl)cyclohexyl)methyl)propanamide)
428876-74-8 ((S)-2-((Benzo[c]-1,2,5-oxadiazol-4-ylsulfonyl)amino)-3-(1H-indol-3-yl)-2-methyl-N-((1-(pyridin-2-yl)cyclohexyl)methyl)propanamide)
25506-37-0 ((4-Methoxyphenyl)methyl 4-nitrophenyl carbonate)
31558-54-0 ((3,4-Dimethoxyphenyl)methyl 4-nitrophenyl carbonate)
73717-05-2 ((2-Chlorophenyl)methyl 4-nitrophenyl carbonate)
97534-88-8 ((4-Chlorophenyl)methyl 4-nitrophenyl carbonate)

. . .

L7 ANSWER 20 OF 25 PROMT COPYRIGHT 2004 Gale Group on STN

AB Following is a summary of news releases transmitted this morning by PR Newswire. The full text of these releases is available at the PRN Press Room, http://www.prnmedia.com.
THIS IS THE FULL TEXT: COPYRIGHT 2001 PR Newswire Association, Inc.

ACCESSION NUMBER: 2001:494299 PROMT
TITLE: PR Newswire National Summary, Thurs.,June 28, 2001 from 8 to 10 A.M. EST.
SOURCE: PR Newswire, (28 Jun 2001) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 3845
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX NETH012 06/28/2001 09:06 r f bc-NJ-Kelsey-**Grp**-predict (BOSTON) MacroChem Highlights Topical **Erectile-Dysfunction** Drug

L7 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for determining the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for determining the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS **dysfunctions**, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social

consequences of brain injury; psychotic disorders and personality disorders; dementia and/or associated syndromes; cardiovascular disease, **dysfunction** and damage; **dysfunction**, damage or disease of the gastrointestinal tract; **dysfunction**, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; **dysfunction**, damage or disease of the body as an abnormal development process; **dysfunction**, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic **dysfunction**, damage or disease; headaches or **sexual dysfunction**. This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

ACCESSION NUMBER: 2001:828425 CAPLUS
DOCUMENT NUMBER: 137:89413
TITLE: Detection of variations in the DNA methylation profile of genes in the determining the risk of disease
INVENTOR(S): Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander
PATENT ASSIGNEE(S): Epigenomics A.-G., Germany
SOURCE: PCT Int. Appl., 636 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 68
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077373	A2	20011018	WO 2001-XB1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GW, ML, MR, NE, SN, TD, TG				
DE 10019058	A1	20011220	DE 2000-10019058	20000406
WO 2001077373	A2	20011018	WO 2001-DE1486	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1274865	A2	20030115	EP 2001-953936	20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531589	T2	20031028	JP 2001-575634	20010406
EP 1360319	A2	20031112	EP 2001-955278	20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003162194	A1	20030828	US 2003-240452	20030414
JP 2004008217	A2	20040115	JP 2003-160375	20030605

US 2004023279 A1 20040205 US 2003-455212 20030605
PRIORITY APPLN. INFO.: DE 2000-10019058 A 20000406
WO 2001-DE1486 W 20010406
DE 2000-10019173 A 20000407
DE 2000-10032529 A 20000630
DE 2000-10043826 A 20000901
WO 2001-EP3969 W 20010406
WO 2001-EP4016 W 20010406
EP 2002-90203 A 20020605

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for determining the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for determining the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS **dysfunctions**, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or associated syndromes; cardiovascular disease, **dysfunction** and damage; **dysfunction**, damage or disease of the gastrointestinal tract; **dysfunction**, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; **dysfunction**, damage or disease of the body as an abnormal development process; **dysfunction**, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic **dysfunction**, damage or disease; headaches or **sexual dysfunction**. This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

IT Amelogenins
Arrestins
CD14 (antigen)
CD19 (antigen)
CD2 (antigen)
CD20 (antigen)
CD22 (antigen)
CD26 (antigen)
CD28 (antigen)
CD3 (antigen)
CD30 (antigen)
CD34 (antigen)
CD38 (antigen)
CD40 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD59 (antigen)
CD68 (antigen)
CD69 (antigen)
CD7 (antigen)
CD8 (antigen)
CD80 (antigen)
CD86 (antigen)
Corticosteroid receptors
Desmins

Elastins
Gastrin-releasing peptide receptors
Gelsolin
Glucagon-like peptide-1 receptors
Gonadotropin-releasing hormone receptor
Hepatocyte growth factor
Immunoglobulin receptors
Intrinsic factors
Invariant chain (class II antigen)
LFA-3 (antigen)
Leukosialin
Metallothioneins
Moesins
Monocyte chemoattractant protein-1
Mucins
Prolamins
Thyroglobulin
Titins
Transferrin receptors
Villin
c-Kit (protein)
α-Fetoproteins
α1-Acid glycoprotein
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA methylation profiles in gene for and disease susceptibility; detection of variations in DNA methylation profile of genes in determining risk of disease)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type BB2, DNA methylation profiles in gene for and disease susceptibility; detection of variations in DNA methylation profile of genes in determining risk of disease)

L7 ANSWER 22 OF 25 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 6
AB The present invention relates to methods of treating obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia using a neurotensin receptor ligand. The present invention also relates to pharmaceutical compositions and kits that comprise a neurotensin receptor ligand.
CLMN 16
AN 10046798 IFIPAT;IFIUDB;IFICDB
TITLE: METHODS OF TREATING OBESITY USING A NEUROTENSIN RECEPTOR LIGAND; MAY CONTAIN ANOTHER COMPOUND TO TREAT DIABETES, **SEXUAL DYSFUNCTION**, ATHEROSCLEROSIS, INSULIN RESISTANCE, IMPAIRED GLUCOSE TOLERANCE, HYPERCHOLESTEROLEMIA OR HYPERTRIGLYCERIDEMIA
INVENTOR(S): Hadcock; John R., East Lyme, CT, US
PATENT ASSIGNEE(S): Unassigned
AGENT: Gregg C. Benson Pfizer Inc., Patent Department, MS 4159, Eastern Point Road, Groton, CT, 06340, US

NUMBER	PK	DATE

09/700,165

PATENT INFORMATION: US 2001046956 A1 20011129
APPLICATION INFORMATION: US 2001-841276 20010424

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2000-199951P	20000427 (Provisional)
FAMILY INFORMATION:	US 2001046956	20011129

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
NUMBER OF CLAIMS: 16

TI METHODS OF TREATING OBESITY USING A NEUROTENSIN RECEPTOR LIGAND; MAY CONTAIN ANOTHER COMPOUND TO TREAT DIABETES, **SEXUAL DYSFUNCTION**, ATHEROSCLEROSIS, INSULIN RESISTANCE, IMPAIRED GLUCOSE TOLERANCE, HYPERCHOLESTEROLEMIA OR HYPERTRIGLYCERIDEMIA

AB The present invention relates to methods of treating obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia using a neurotensin receptor ligand. The present invention also relates to. . .

ACLM . . . a compound that is a neurotensin receptor ligand; and b) a second compound useful for the treatment of obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia.

. . . cannabinoid receptor antagonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . .

. . . neurotensin receptor ligand; b) a second pharmaceutical composition comprising a compound that is useful for the treatment of obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia; and c) a container for the first and second compositions.

. . . cannabinoid receptor antagonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a **bombesin** agonist, a neuropeptide-Y antagonist, a thyromimetic agent, dehydroepiandrosterone or an analog thereof, a glucocorticoid receptor agonist or antagonist, an orexin. . .

15. A method of treating diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia, the method comprising the step of administering to a patient having or at risk of having, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertrigylceridemia a therapeutically effective amount of a neurotensin receptor ligand.

L7 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN

AB Methods are provided for treating obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertriglyceridemia using a neurotensin receptor ligand. The invention also provides pharmaceutical compns. and kits that comprise a neurotensin receptor ligand.

ACCESSION NUMBER: 2001:864708 CAPLUS
DOCUMENT NUMBER: 136:693
TITLE: Method using a neurotensin receptor ligand for treating obesity and other disorders
INVENTOR(S): Hadcock, John Richard Neville
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1157695	A1	20011128	EP 2001-303855	20010427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046956	A1	20011129	US 2001-841276	20010424
CA 2345180	AA	20011027	CA 2001-2345180	20010425
ZA 2001003365	A	20021025	ZA 2001-3365	20010425
NZ 511354	A	20030328	NZ 2001-511354	20010426
JP 2002275092	A2	20020925	JP 2001-130680	20010427

PRIORITY APPLN. INFO.: US 2000-199951P P 20000427
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Methods are provided for treating obesity, diabetes, **sexual dysfunction**, atherosclerosis, insulin resistance, impaired glucose tolerance, hypercholesterolemia or hypertriglyceridemia using a neurotensin receptor ligand. The invention also provides pharmaceutical compns. and kits that comprise a neurotensin receptor ligand.

ST neurotensin receptor ligand obesity diabetes atherosclerosis; **sexual dysfunction** hypercholesterolemia neurotensin receptor ligand; insulin resistance hypertriglyceridemia neurotensin receptor ligand; glucose tolerance impairment neurotensin receptor ligand

IT 9011-97-6, Cholecystokinin 31362-50-2, **Bombesin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; neurotensin receptor ligand for treating obesity and other disorders, and use with other agents)

L7 ANSWER 24 OF 25 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-558005 [63] WPIDS
AB CA 2332169 A UPAB: 20021031
NOVELTY - A composition (A) comprises a compound (I) that attenuates the binding of agouti-related protein to melanocortin receptors, but does not attenuate the binding of alpha -melanocyte stimulating hormone to melanocortin receptors and optionally a compound (ii) that is melanocortin receptor agonist.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a drug comprising (I) and carrier or diluent and optionally (II);

(2) a kit comprising (I), a composition containing (II) and a container for the two compositions;

(3) a commercial package comprising the drug and a written matter which describes instructions for using the drug; and

(4) identifying a compound useful for treating obesity, **sexual dysfunction**, diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal **dysfunction**, hypertension,

hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia or substance abuse involving: a) determining if a compound affects the binding of agouti-related protein to melanocortin receptors, b) determining if a compound affects the binding of alpha -melanocyte stimulating hormone to melanocortin receptors and selecting (I).

ACTIVITY - Anorectic; Vasotropic; Antidiabetic; Hypotensive; Antilipemic; Antiarteriosclerotic; Antiaddictive.

MECHANISM OF ACTION - Agouti-related protein (AGRP) inhibitor or alpha -melanocyte stimulating hormone (alpha -MSH) inhibitor.

Details of radioligand binding assays are given, but no biological data is given.

USE - For treating obesity, **sexual dysfunction** (e.g. **erectile dysfunction**), diabetes (e.g. non-insulin dependent diabetes mellitus), insulin resistance, hyperinsulinemia, Syndrome X, adrenal **dysfunction**, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia or substance abuse (e.g. alcohol abuse) (all claimed).

ADVANTAGE - Compound (I) attenuates the binding of agouti-related protein to melanocortin receptors, but does not attenuate the binding of alpha -melanocyte stimulating hormone to melanocortin receptors.

Dwg.0/0

ACCESSION NUMBER: 2001-558005 [63] WPIDS
DOC. NO. CPI: C2001-166045
TITLE: Composition for treating e.g. **sexual dysfunction** comprises a compound for attenuating the binding of agouti-related protein to melanocortin receptors without attenuating the binding of melanocyte stimulating hormone to receptors.
DERWENT CLASS: B05
INVENTOR(S): HADCOCK, J R N; SWICK, A G; HADCOCK, J R
PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC; (HADC-I) HADCOCK J R; (SWIC-I) SWICK A G; (PFIZ) PFIZER INC
COUNTRY COUNT: 30
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2332169	A1	20010718	(200163)*	EN	57
BR 2001000106	A	20010828	(200163)		
EP 1125579	A2	20010822	(200163)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
JP 2001242173	A	20010907	(200166)		27
US 2002065277	A1	20020530	(200240)		
US 6451783	B1	20020917	(200264)		
US 2002198152	A1	20021226	(200304)		
JP 3487591	B2	20040119	(200410)		26
JP 2004053602	A	20040219	(200414)		39

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2332169	A1	CA 2001-2332169	20010116
BR 2001000106	A	BR 2001-106	20010118

EP 1125579	A2		EP 2001-300233	20010111
JP 2001242173	A		JP 2001-9643	20010118
US 2002065277	A1	Provisional	US 2000-176508P	20000118
		Provisional	US 2000-206126P	20000522
			US 2001-761320	20010116
US 6451783	B1	Provisional	US 2000-176508P	20000118
		Provisional	US 2000-206126P	20000522
			US 2001-761320	20010116
US 2002198152	A1	Provisional	US 2000-176508P	20000118
		Provisional	US 2000-206126P	20000522
		Div ex	US 2001-761320	20010116
			US 2002-205304	20020724
JP 3487591	B2		JP 2001-9643	20010118
JP 2004053602	A	Div ex	JP 2001-9643	20010118
			JP 2003-193983	20030709

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2002198152	A1	Div ex	US 6451783
JP 3487591	B2	Previous Publ.	JP 2001242173

PRIORITY APPLN. INFO: US 2000-206126P 20000522; US 2000-176508P 20000118; US 2001-761320 20010116; US 2002-205304 20020724

TI Composition for treating e.g. **sexual dysfunction** comprises a compound for attenuating the binding of agouti-related protein to melanocortin receptors without attenuating the binding of melanocyte stimulating. . .

AB . . .

and a written matter which describes instructions for using the drug; and

(4) identifying a compound useful for treating obesity, **sexual dysfunction**, diabetes, insulin resistance, hyperinsulinemia, Syndrome X, adrenal **dysfunction**, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia or substance abuse involving: a) determining if a compound affects the binding of agouti-related protein. . . inhibitor.

Details of radioligand binding assays are given, but no biological data is given.

USE - For treating obesity, **sexual dysfunction** (e.g. **erectile dysfunction**), diabetes (e.g. non-insulin dependent diabetes mellitus), insulin resistance, hyperinsulinemia, Syndrome X, adrenal **dysfunction**, hypertension, hypercholesterolemia, atherosclerosis, hyperlipoproteinemia, hypertriglyceridemia or substance abuse (e.g. alcohol abuse) (all claimed).

ADVANTAGE - Compound (I) attenuates the. . .

TECH. . .

hormone receptor analog, cannabinoid receptor antagonist, melanin concentrating hormone antagonist, leptin, leptin analog, leptin receptor agonist, galanin antagonist, lipase inhibitor, **bombesin** agonist, neuropeptide-Y antagonist, thyromimetic agent, dehydroepiandrosterone or their analog, glucocorticoid receptor agonist or antagonist, orexin receptor antagonist, urocortin binding protein. . .

L7 ANSWER 25 OF 25 PROMT COPYRIGHT 2004 Gale Group on STN

AB CGTU044 11/14/2000 10:01 r l bc-IL-Mid-America-Promot (CHICAGO) The World's Largest Indoor Chevrolet and Corvette Car Show, Car Sale, and Swap Meet Will Be Held Saturday, November 18th and Sunday, November 19th
THIS IS THE FULL TEXT: COPYRIGHT 2000 PR Newswire Association, Inc.

ACCESSION NUMBER: 2000:1001632 PROMT
TITLE: PR Newswire National Summary, Tuesday, November 14, 10:00 A.M. EDT to Noon.
SOURCE: PR Newswire, (14 Nov 2000) .
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 3637
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX LATU090 11/14/2000 10:04 r f bc-CA-S.B-Restaurant-**Grp** (SANTA BARBARA) Santa Barbara Restaurant Group Completes Divestiture of JB's Family Restaurants, Inc.
NETU031 11/14/2000 11:46 r f bc-MA-Decision-Resources (WALTHAM) Decision Resources Study Evaluates the Commercial Potential of Current and Emerging Therapies to Treat **Erectile Dysfunction**

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DELACROIX

15 FILES SEARCHED...
L2 56973 L1

=> s l2 and (libido? or anorgasm? or vaginismu? or dyspareuni? or impoten?)
L3 18 L2 AND (LIBIDO? OR ANORGASM? OR VAGINISMU? OR DYSPAREUNI? OR IMPOTEN?)

=> dup rem l3
DUPLICATE IS NOT AVAILABLE IN 'DGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L3
L4 15 DUP REM L3 (3 DUPLICATES REMOVED)

=> d l4 abs ibib kwic 1-15

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
AB Methods of improving the permeability of mucosal epithelia to improve the efficiency of transmucosal delivery of drugs are described. Permeability is improved by modulating epithelial junction structure or physiol. of the mucosa using a peptide derived from one of the proteins involved in the junction, such as junctional adhesion mols. (JAMs), occludins, or claudins. The permeabilizing agent is typically a peptide or peptide analog or mimetic, often selected or derived from an extracellular domain of a mammalian JAM, occludin or claudin protein. Identification of candidate peptides derived from junctional adhesion mol. JAM-1, claudins and occludins is demonstrated. The effects of the peptides were tested in a com. airway epithelium model. Tests in adult male volunteers showed a significant improvement in the delivery of human interferon β across the nasal mucosa when a peptide derived from JAM-1 was included in an intranasal formulation.

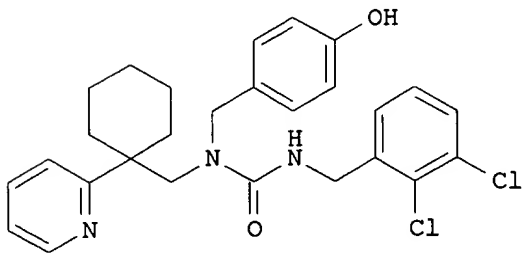
ACCESSION NUMBER: 2004:20807 CAPLUS
DOCUMENT NUMBER: 140:99589
TITLE: Use of peptides derived from junctional adhesion molecules to permeabilize mucosa for improved efficiency of mucosal delivery of therapeutic compounds
INVENTOR(S): Quay, Steven C.
PATENT ASSIGNEE(S): Nastech Pharmaceutical Company, Inc., USA
SOURCE: PCT Int. Appl., 426 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004003145	A2	20040108	WO 2003-US19994	20030624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,

GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-392512P P 20020628
IT Sexual behavior
(**impotence**, treatment of; use of peptides derived from junctional adhesion mols. to permeabilize mucosa for improved efficiency of mucosal delivery of therapeutic compds.)
IT 50-22-6, Corticosterone 50-56-6, Oxytocin, biological studies 51-34-3, Scopolamine 52-39-1, Aldosterone 57-83-0, Progestin, biological studies 58-22-0, Testosterone 137-58-6, Lidocaine 141-43-5, Olamine, biological studies 301-02-0, Oleamide 548-73-2, Droperidol 9000-81-1, Acetylcholinesterase 9000-96-8, Arginase 9001-26-7, Prothrombin 9001-73-4, Papain 9002-07-7, Trypsin 9002-60-2, ACTH, biological studies 9002-62-4, Prolactin, biological studies 9002-64-6, Parathormone 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyroid stimulating hormone 9002-72-6, Somatotropin 9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies 9005-49-6, Heparin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9015-68-3, Asparaginase 9026-93-1, Adenosine deaminase 9027-98-9 9031-37-2, Ceruloplasmin 9034-40-6, LHRH 9038-70-4, Somatomedin 9054-89-1, Superoxide dismutase 9061-61-4, Nerve growth factor 9088-07-7, Natriuretic peptide 11000-17-2, Vasopressin 11096-26-7, Erythropoietin 15826-37-6, Cromolyn sodium 22071-15-4, Ketoprofen 23031-25-6, Terbutaline 29342-05-0, Ciclopirox 31362-50-2, **Bombesin** 33507-63-0, Substance P 33515-09-2, Gonadorelin 36505-84-7, Buspirone 37025-55-1, Carbetocin 37213-49-3, α-MSH 37221-79-7, Vasoactive intestinal peptide 51110-01-1, Somatostatin 51481-61-9, Cimetidine 56030-54-7 59467-70-8, Midazolam 60118-07-2, Endorphin 62229-50-9, Epidermal growth factor 62571-86-2, Captopril 66357-35-5, Ranitidine 76547-98-3, Lisinopril 76824-35-6, Famotidine 79217-60-0, Cyclosporin 83435-66-9, Delapril 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 139639-23-9, Tissue plasminogen activator 152166-55-7, Adenosine deaminase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery across mucosa of; use of peptides derived from junctional adhesion mols. to permeabilize mucosa for improved efficiency of mucosal delivery of therapeutic compds.)

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB R1(CH2)mCR3R4(CH2)nY(CH2)pCO(CH2)qNH(CH2)rR2 [R1 = (un)substituted aryl, heteroaryl, CO2H, CONH2, NH2, OH, alkyl, cycloalkyl; M, n, p, q = 0-2; r = 0-4; Y = (un)substituted NH, CH2; R2 = (un)substituted cycloalkyl, aryl,

heteroaryl, aryloxy, alkyl, adamantyl, alkenyl; R3, R4 = H, alkyl; R3R4 = alkylene, heteroalkylene] were prepared for use as **bombesin** antagonists in treatment of male and female sexual dysfunction, particularly female sexual arousal disorder and male erectile dysfunction. Thus, 2-pyridinylacetonitrile was treated with Br(CH2)5Br to give 1-(2-pyridinyl)cyclohexylacetonitrile which was reduced to the amine, reductively alkylated with 4-HOC6H4CHO, and treated with 2,3-Cl2C6H3NH2 and triphosgene to give the urea I. I has Ki 82 nM for antagonism at the BB1 receptor.

ACCESSION NUMBER: 2003:892600 CAPLUS
DOCUMENT NUMBER: 139:381374
TITLE: Preparation of urea derivatives as **bombesin** antagonists
INVENTOR(S): Higginbottom, Michael; Kesten, Suzanne Ross; Lewthwaite, Russell Andrew; Pritchard, Martyn Clive; Rawson, David James; Schelkun, Robert Michael; Yuen, Po-Wai
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 227 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092670	A1	20031113	WO 2003-IB1686	20030417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-10239 A 20020503
US 2002-398132P P 20020723
OTHER SOURCE(S): MARPAT 139:381374
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of urea derivatives as **bombesin** antagonists

AB R1(CH2)mCR3R4(CH2)nY(CH2)pCO(CH2)qNH(CH2)rR2 [R1 = (un)substituted aryl, heteroaryl, CO2H, CONH2, NH2, OH, alkyl, cycloalkyl; M, n, p, q = 0-2; r = 0-4; Y = (un)substituted NH, CH2; R2 = (un)substituted cycloalkyl, aryl, heteroaryl, aryloxy, alkyl, adamantyl, alkenyl; R3, R4 = H, alkyl; R3R4 = alkylene, heteroalkylene] were prepared for use as **bombesin** antagonists in treatment of male and female sexual dysfunction, particularly female sexual arousal disorder and male erectile dysfunction. Thus, 2-pyridinylacetonitrile was treated with Br(CH2)5Br to give 1-(2-pyridinyl)cyclohexylacetonitrile which was reduced to the amine, reductively alkylated with 4-HOC6H4CHO, and treated with 2,3-Cl2C6H3NH2 and triphosgene to give the urea I. I has Ki 82 nM for antagonism at the BB1 receptor.

ST urea prepn **bombesin** antagonist sexual dysfunction

IT Mental disorder
(affective, seasonal; preparation of urea derivs. as **bombesin** antagonists)

IT Mental disorder
(depression; preparation of urea derivs. as **bombesin** antagonists)

IT Sexual behavior
(disorder, female; preparation of urea derivs. as **bombesin** antagonists)

IT Appetite
Sleep
(disorder; preparation of urea derivs. as **bombesin** antagonists)

IT Porphyria
(hepatic; preparation of urea derivs. as **bombesin** antagonists)

IT Sexual behavior
(**impotence**; preparation of urea derivs. as **bombesin** antagonists)

IT Anxiety
(panic disorder; preparation of urea derivs. as **bombesin** antagonists)

IT Analgesics
Anorexia
Antidepressants
Antiemetics
Antipsychotics
Antitumor agents
Anxiety
Anxiolytics
Digestive tract, disease
Human
Pain
Pancreas, neoplasm
Prostate gland, neoplasm
Vomiting
(preparation of urea derivs. as **bombesin** antagonists)

IT Mental disorder
(psychosis; preparation of urea derivs. as **bombesin** antagonists)

IT Hypertension
(pulmonary; preparation of urea derivs. as **bombesin** antagonists)

IT Memory, biological
(retention defect; preparation of urea derivs. as **bombesin** antagonists)

IT Anxiety
(social; preparation of urea derivs. as **bombesin** antagonists)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1; preparation of urea derivs. as **bombesin** antagonists)

IT 623567-69-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. as **bombesin** antagonists)

IT 51-67-2, 4-(2-Aminoethyl)phenol 66-99-9, 2-Naphthaldehyde 78-84-2, Isobutyraldehyde 78-96-6, 1-Amino-2-propanol 90-02-8, Salicylaldehyde, reactions 93-53-8, 2-Phenylpropanal 95-00-1, 2,4-Dichlorobenzylamine 95-01-2, 2,4-Dihydroxybenzaldehyde 96-34-4, Methyl chloroacetate 96-48-0, γ-Butyrolactone 98-01-1, Furfural, reactions 98-03-3,

2-Thiophenecarboxaldehyde 99-61-6, 3-Nitrobenzaldehyde 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-82-3, 3-Fluorobenzylamine 100-83-4, 3-Hydroxybenzaldehyde 101-39-3, α-Methylcinnamaldehyde 102-49-8, 3,4-Dichlorobenzylamine 104-86-9, 4-Chlorobenzylamine 105-07-7, 4-Formylbenzonitrile 107-11-9, Allylamine 108-00-9, N,N-Dimethylethylenediamine 109-01-3, 1-Methylpiperazine 111-24-0, 1,5-Dibromopentane 118-31-0, 1-Naphthylmethylamine 121-33-5, Vanillin 122-85-0, 4-Acetylaminobenzaldehyde 123-08-0, 4-Hydroxybenzaldehyde 123-11-5, 4-Methoxybenzaldehyde, reactions 140-29-4, Phenylacetonitrile 151-18-8, 3-Aminopropionitrile 156-87-6, 3-Amino-1-propanol 405-05-0, 3-Fluoro-4-hydroxybenzaldehyde 447-61-0, 2-Trifluoromethylbenzaldehyde 454-89-7, 3-Trifluoromethylbenzaldehyde 455-19-6, 4-Trifluoromethylbenzaldehyde 460-40-2, 3,3,3-Trifluoropropanal 500-22-1, 3-Pyridinecarboxaldehyde 616-30-8, 3-Amino-1,2-propanediol 619-21-6, 3-Formylbenzoic acid 621-59-0, Isovanillin 629-03-8, 1,6-Dibromohexane 643-28-7, 2-Isopropylaniline 654-01-3, 2,6-Difluorophenylacetonitrile 704-13-2, 3-Hydroxy-4-nitrobenzaldehyde 753-90-2, 2,2,2-Trifluoroethylamine 766-05-2, Cyclohexanecarbonitrile 867-13-0, Triethyl phosphonoacetate 872-85-5, 4-Pyridinecarboxaldehyde 873-74-5, 4-Cyanoaniline 929-06-6, 2-(2-Aminoethoxy)ethanol 1003-29-8, 2-Formylpyrrole 1121-60-4, 2-Pyridinecarboxaldehyde 1130-21-8 1192-58-1, 2-Formyl-1-methylpyrrole 1194-98-5, 2,5-Dihydroxybenzaldehyde 1210-39-5, 3,3-Diphenyl-2-propenal 1489-69-6, Cyclopropanecarboxaldehyde 1532-84-9, 1-Aminoisoquinoline 1571-08-0, Methyl 4-formylbenzoate 1641-09-4, 3-Thiophenecarbonitrile 1648-99-3, 2,2,2-Trifluoroethanesulfonyl chloride 1711-11-1, 3-Cyanobenzoyl chloride 1758-46-9, 2-Phenoxyethylamine 1859-37-6 1899-24-7, 5-Bromofurfural 2233-18-3, 4-Hydroxy-3,5-dimethylbenzaldehyde 2314-36-5, 3,5-Dichloro-4-hydroxybenzaldehyde 2393-23-9, 4-Methoxybenzylamine 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 2450-26-2, 4-Hydroxy3-methoxy-2-nitrobenzaldehyde 2450-71-7, Propargylamine 2508-29-4, 5-Amino-1-pentanol 2612-57-9, 2,4-Dichlorophenyl isocyanate 2739-97-1, 2-Pyridinylacetonitrile 2740-83-2, 3-Trifluoromethylbenzylamine 3011-34-5, 4-Hydroxy-3-nitrobenzaldehyde 3048-01-9, 2-Trifluoromethylbenzylamine 3182-95-4 3216-48-6, Benzo[b]thiophene-3-acetonitrile 3218-02-8, Cyclohexylmethanamine 3235-69-6, 4-Morpholinylacetic acid 3886-69-9 3886-70-2 4363-93-3, Quinoline-4-carboxaldehyde 4397-53-9, 4-Benzyloxybenzaldehyde 4414-88-4, 2-Benzimidazoleacetonitrile 4530-20-5, N-tert.-Butoxycarbonylglycine 4701-17-1, 5-Bromo-2-thiophenecarboxaldehyde 5071-96-5, 3-Methoxybenzylamine 5084-46-8, 6-Methyl-2-naphthaldehyde 5414-19-7, Bis(2-bromoethyl) ether 5437-45-6, Benzyl bromoacetate 5544-60-5, 4-Benzyloxybenzyl bromide 5558-29-2, 3-Methyl-2-phenylbutyronitrile 5834-16-2, 3-Methyl-2-thiophenecarboxaldehyde 6361-21-3, 2-Chloro-5-nitrobenzaldehyde 6745-75-1, 4-Methoxy-2,5-dimethylbenzaldehyde 6850-57-3, 2-Methoxybenzylamine 7035-03-2, 2-Methoxyphenylacetonitrile 7175-81-7 7202-43-9 7451-95-8, 2-Hydroxy-2-phenylethanal 10111-08-7, 1H-Imidazole-2-carboxaldehyde 10551-58-3, 5-Acetoxymethylfurfural 13049-86-0 13325-10-5, 4-Amino-1-butanol 13679-70-4, 5-Methyl-2-thiophenecarboxaldehyde 14510-06-6, 8-Hydroxy-quinoline-2-carboxaldehyde 15174-69-3, 4-Hydroxy-3-methylbenzaldehyde 17337-13-2, 2-Isocyanato-1,1'-Biphenyl 18278-34-7, 4-Hydroxy-2-methoxybenzaldehyde 18542-42-2, 2-Methylthioethylamine 20458-99-5, 2,6-Diethylphenyl isocyanate 24437-41-0 24544-04-5, 2,6-Diisopropylaniline 24677-78-9, 2,3-Dihydroxybenzaldehyde 24964-64-5, 3-Formylbenzonitrile 26507-91-5,

2-Methoxy-3-methylbenzoic acid 27996-87-8, 2-Fluoro-5-nitrobenzaldehyde 28178-42-9, 2,6-Diisopropylphenyl isocyanate 29668-44-8, 1,4-Benzodioxane-6-carboxaldehyde 30084-91-4, Indan-5-carboxaldehyde 31027-31-3, 4-Isopropylphenyl isocyanate 34296-51-0, 1-Phenyl-1,2,3-triazole-4-carboxaldehyde 34967-24-3, 3,5-Dimethoxybenzylamine 36268-67-4 37748-09-7, 3-Formylphenoxyacetic acid 39226-95-4, 2,3-Dichlorobenzylamine 42340-98-7 42454-06-8, 5-Hydroxy-2-nitrobenzaldehyde 50528-73-9, 4-Benzyloxyphenyl isocyanate 51586-20-0, 2,3-Dimethylbenzylamine 52178-50-4, Methyl 3-formylbenzoate 52771-21-8, 3-Trifluoromethoxybenzaldehyde 56278-50-3, 2-Benzothiazoleacetonitrile 56962-11-9, 2-Chloro-4-hydroxybenzaldehyde 59566-45-9, 2-Pyrimidineacetonitrile 60345-97-3, 3-(2-Hydroxyethoxy)benzaldehyde 60656-87-3, 2-Benzyloxyethanal 61587-91-5 62327-21-3, tert.Butyl dimethyl phosphonoacetate 68282-47-3, 2-Phenyl-1H-imidazole-4-carboxaldehyde 71189-14-5, 2-Adamantyl isocyanate 73568-25-9, 2-Chloroquinoline-3-carboxaldehyde 75428-45-4, 2-Nitro-4-thiophenecarboxaldehyde 76874-79-8, 2-Amino-4-chlorothiazole-5-carboxaldehyde 92972-48-0, 2,4-Dichlorothiazole-5-carboxaldehyde 98550-45-9 99856-75-4 102561-41-1 102561-43-3, 2-Isopropyl-6-methylphenyl isocyanate 106429-59-8 120949-66-8 175203-90-4 175204-81-6, 4-Chloro-1-methyl-1H-pyrazole-3-carboxaldehyde 175277-27-7 184434-21-7 200195-19-3 201531-21-7 204067-12-9 623570-11-6 623570-54-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of urea derivs. as **bombesin** antagonists)

IT 1202-81-9P 3441-01-8P 14006-32-7P 33322-63-3P 36263-42-0P 50654-43-8P 54699-92-2P 74815-33-1P 83922-54-7P 90609-90-8P 91284-60-5P 94239-10-8P 126534-87-0P 126926-36-1P 126926-39-4P 137864-55-2P 168433-01-0P 182740-44-9P 183739-65-3P 196106-01-1P 204067-08-3P 204067-32-3P 204514-23-8P 363186-09-8P 425641-34-5P 425641-45-8P 581102-27-4P 623569-55-1P 623569-56-2P 623569-57-3P 623569-58-4P 623569-59-5P 623569-60-8P 623569-61-9P 623569-62-0P 623569-63-1P 623569-64-2P 623569-65-3P 623569-66-4P 623569-67-5P 623569-68-6P 623569-69-7P 623569-70-0P 623569-71-1P 623569-72-2P 623569-73-3P 623569-74-4P 623569-75-5P 623569-76-6P 623569-77-7P 623569-78-8P 623569-79-9P 623569-80-2P 623569-81-3P 623569-82-4P 623569-83-5P 623569-84-6P 623569-85-7P 623569-86-8P 623569-87-9P 623569-88-0P 623569-89-1P 623569-90-4P 623569-91-5P 623569-92-6P 623569-93-7P 623569-94-8P 623569-95-9P 623569-96-0P 623569-97-1P 623569-98-2P 623569-99-3P 623570-00-3P 623570-01-4P 623570-02-5P 623570-03-6P 623570-04-7P 623570-05-8P 623570-06-9P 623570-07-0P 623570-08-1P 623570-09-2P 623570-10-5P 623570-12-7P 623570-13-8P 623570-14-9P 623570-15-0P 623570-16-1P 623570-17-2P 623570-18-3P 623570-19-4P 623570-20-7P 623570-21-8P 623570-22-9P 623570-23-0P 623570-24-1P 623570-25-2P 623570-26-3P 623570-27-4P 623570-28-5P 623570-29-6P 623570-30-9P 623570-31-0P 623570-32-1P 623570-33-2P 623570-34-3P 623570-35-4P 623570-36-5P 623570-37-6P 623570-38-7P 623570-39-8P 623570-40-1P 623570-41-2P 623570-42-3P 623570-43-4P 623570-44-5P 623570-45-6P 623570-46-7P 623570-47-8P 623570-48-9P 623570-49-0P 623570-50-3P 623570-51-4P 623570-52-5P 623570-53-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of urea derivs. as **bombesin** antagonists)

IT 623567-98-6P 623567-99-7P 623568-01-4P 623568-02-5P 623568-07-0P 623568-96-7P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

USES (Uses)
(preparation of urea derivs. as **bombesin** antagonists)

IT 623567-70-4P 623567-71-5P 623567-72-6P 623567-73-7P 623567-74-8P
623567-75-9P 623567-76-0P 623567-77-1P 623567-78-2P 623567-79-3P
623567-80-6P 623567-81-7P 623567-82-8P 623567-83-9P 623567-84-0P
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623569-36-8P 623569-37-9P 623569-38-0P 623569-39-1P 623569-40-4P
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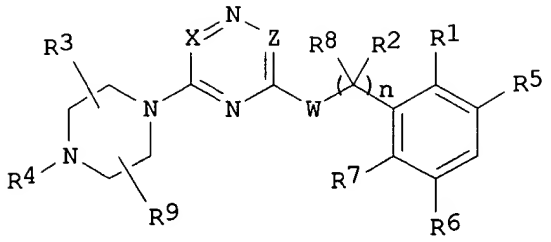
623569-46-0P 623569-47-1P 623569-48-2P 623569-49-3P 623569-50-6P
623569-51-7P 623569-52-8P 623569-53-9P 623569-54-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. as **bombesin** antagonists)

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
GI



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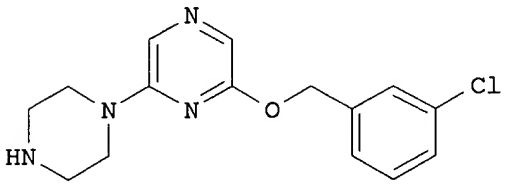


II

AB Title compds. (I) [wherein X and Z = independently CR; R = H, halo, alkyl(amino), or amino; W = O, S, NH, alkylamino, or acetylamino; at least one of R1, R5, R6, or R7 = independently halo, NO2, (alkyl)amino, CN, CONH2, (halo)alkyl, or alkoxy; or C2R1R5 = 5- or 6-membered aromatic or fused ring; or R1 taken together with R2 or R8 forms a 5- or 6-membered fused ring; R2 and R8 = independently H or (cyclo)alkyl; n = 0-2; R3 and R9 = independently H, halo, alkyl, or alkyl substituted with OH, F, or alkoxy; R4 = H, OH, (hydroxy)alkyl, cyanoalkyl, alkylcarbonyl, alkoxy(carbonyl), or alkenyl; or N-oxides, prodrugs, pharmaceutically acceptable salts, solvates, or hydrates thereof] were prepared as 5-hydroxytryptamine (5-HT) receptor ligands, in particular 5-HT2C receptor ligands. For instance, 2,6-dichloropyrazine was coupled with piperazine-1-carboxylic acid tert-Bu ester using Na2CO3 in t-BuOH to give 6'-chloro-2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-carboxylic acid tert-Bu ester. Substitution with 3-chlorobenzyl alc. in the presence of KOH and 18-crown-6 in toluene followed by deesterification afforded 6'-(3-chlorobenzyloxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl (II). Compds. of the invention demonstrated affinity at the serotonin 5HT2A and 5HT2C binding sites with Ki values ranging from 0.5 nM to 1.0 μM and 0.1 nM to 586.5 nM, resp. In a functional assay using 5-HT2C expressed NIH 3T3 cells, II displayed EC50 ≤ 1.0 μM. I and pharmaceutical compns. containing I are useful for the treatment of diseases linked to the activation of 5-HT2 receptors, such as sexual dysfunction (no data).

ACCESSION NUMBER: 2003:5937 CAPLUS
DOCUMENT NUMBER: 138:73273
TITLE: Preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction
INVENTOR(S): Chiang, Yuan-Ching Phoebe; Dasilva-Jardine, Paul Andrew; Garigipati, Ravi S.; Guzman-Perez, Angel; Novomisle, William Albert; Welch, Willard Mckowan
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000666	A1	20030103	WO 2002-IB2293	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003105106	A1	20030605	US 2002-156884	20020528
US 2003125334	A1	20030703	US 2002-163881	20020605

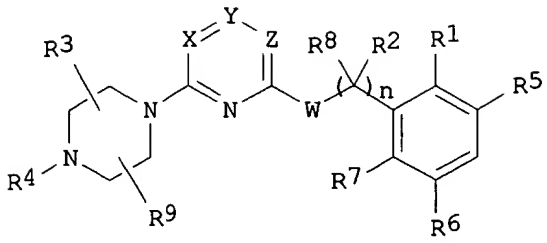
PRIORITY APPLN. INFO.: US 2001-299953P P 20010621
OTHER SOURCE(S): MARPAT 138:73273
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Sexual behavior
(**impotence**; preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)

IT **Bombesin** receptors
Estrogen receptors
Glucocorticoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators, composition component; preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)

IT 111745-44-9, **Neuromedin** U
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists, composition component; preparation of [1,2']bipyrazinyl 5-HT2
receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
GI



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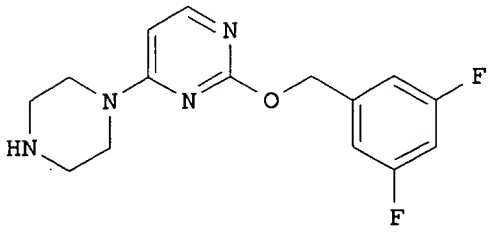

II

AB Title compds. (I) [wherein X and Y = CR and Z = N; or Y and Z = CR and X = N; R = H, halo, alkyl(amino), or amino; W = O, S, NH, alkylamino, or acetylamino; at least one of R1, R5, R6, or R7 = independently halo, NO2, (alkyl)amino, CN, CONH2, (halo)alkyl, or alkoxy; or C2R1R5 = 5- or 6-membered aromatic or fused ring; or R1 taken together with R2 or R8 forms a 5- or 6-membered fused ring; R2 and R8 = independently H or (cyclo)alkyl; n = 0-2; R3 and R9 = independently H, halo, alkyl, or alkyl substituted with OH, F, or alkoxy; R4 = H, OH, (hydroxy)alkyl, cyanoalkyl, alkylcarbonyl, alkoxy(carbonyl), or alkenyl; or N-oxides, prodrugs, pharmaceutically acceptable salts, solvates, or hydrates thereof] were prepared as 5-hydroxytryptamine (5-HT) receptor ligands, in particular 5-HT2C receptor ligands. For example, 2,4-dichloropyrimidine was coupled with piperazine-1-carboxylic acid tert-Bu ester using Na2CO3 in EtOH to give 4-(2-chloropyrimidin-4-yl)piperazine-1-carboxylic acid tert-Bu ester. Substitution with 3,5-difluorobenzyl alc. using NaH in THF afforded 4-[2-(3,5-difluorobenzyloxy)pyrimidin-4-yl]piperazine-1-carboxylic acid tert-Bu ester. Deesterification followed by conversion to the salt produced II•xHCl. Compds. of the invention demonstrated affinity at the serotonin 5HT2A and 5HT2C binding sites with Ki values ranging from 0.5 nM to 625 nM and 0.2 nM to 238 nM, resp. In functional assays, II acted as a partial agonist using 5-HT2A and 5-HT2C expressed NIH 3T3 cells with EC50 values in the range of 0.16 μM to 7.6 μM and 0.016 μM to 7.0 μM, resp. I and pharmaceutical compns. containing I are useful for the treatment of diseases linked to the activation of 5-HT2 receptors, such as sexual dysfunction (no data).

ACCESSION NUMBER: 2003:5934 CAPLUS
DOCUMENT NUMBER: 138:73272
TITLE: Preparation of piperazinylpyrimidines as 5-HT2 receptor ligands for treatment of sexual disorders
INVENTOR(S): Chiang, Yuan-ching Phoebe; Novomisle, William Albert; Welch, Willard Mckowan
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000663	A1	20030103	WO 2002-IB2261	20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003105106	A1	20030605	US 2002-156884	20020528
US 2003125334	A1	20030703	US 2002-163881	20020605

PRIORITY APPLN. INFO.: US 2001-299953P P 20010621
OTHER SOURCE(S): MARPAT 138:73272
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Sexual behavior
(**impotence**; preparation of piperazinylpyrimidine 5-HT2 receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)
IT **Bombesin** receptors
Estrogen receptors
Glucocorticoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators, composition component; preparation of piperazinylpyrimidine 5-HT2
receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Preparation of compds. of the invention is described.
ACCESSION NUMBER: 2002:391522 CAPLUS
DOCUMENT NUMBER: 136:395983
TITLE: **Bombesin** receptor antagonists, and combinations with other agents, for the treatment of sexual dysfunction
INVENTOR(S): Gonzalez, Maria Isabel; Stock, Herman Thijs; Pinnock, Robert Denham; Pritchard, Martyn Clive; Wayman, Christopher Peter; Van der Graaf, Pieter Hadewijn; Naylor, Alisdair Mark; Higginbottom, Michael
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040008	A2	20020523	WO 2001-GB5018	20011114
WO 2002040008	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002040022	A1	20020523	WO 2000-GB4380	20001117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2002023802	A5	20020527	AU 2002-23802	20011114
EP 1333824	A2	20030813	EP 2001-994552	20011114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015364	A	20030923	BR 2001-15364	20011114

PRIORITY APPLN. INFO.:
WO 2000-GB4380 W 20001117
GB 2001-9910 A 20010423
GB 2001-11037 A 20010504
WO 2001-GB5018 W 20011114

OTHER SOURCE(S): MARPAT 136:395983

TI **Bombesin** receptor antagonists, and combinations with other agents, for the treatment of sexual dysfunction

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compds., for example phosphodiesterase V inhibitors, neutral endopeptidase inhibitors, and lasofoxifene. Preparation of compds. of the invention is described.

ST **bombesin** receptor antagonist sexual dysfunction treatment; phosphodiesterase inhibitor **bombesin** antagonist sexual dysfunction treatment; neutral endopeptidase inhibitor **bombesin** antagonist prepn sexual dysfunction treatment; lasofoxifene **bombesin** antagonist sexual dysfunction treatment

IT Nervous system agents
(CNS-active; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Oxytocin receptors
Vasopressin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(agonists and modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT VIP receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Estrogens
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and agonists and antagonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and prostaglandin esters; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT **Gastrin-releasing peptide** receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Behavior
(arousal, sexual arousal disorders; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 5-HT agonists
5-HT antagonists
Angiotensin receptor antagonists
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Dopamine agonists
Drug delivery systems
Drug interactions
Hormone replacement therapy
Human
Opioid antagonists
Platelet aggregation inhibitors
Purinoceptor agonists
Vasodilators
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT **Bombesin** receptors
Sex hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Opioids
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Ion channel blockers
(calcium; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Resolution (separation)
(chromatog.; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Sexual behavior
(disorder; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine-transporting, modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Drugs
(drug-induced sexual dysfunction; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ergot; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Drug delivery systems
(implants, testosterone; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Sexual behavior
(**impotence**; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor, agonists and modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 5-HT receptors
Cannabinoid receptors
Estrogen receptors
Opioid receptors
Potassium channel
Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Anti-inflammatory agents
(nonsteroidal; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine transporter, modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Drug delivery systems
(oral; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT Ion channel openers
(potassium; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin transporter, modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT Antidepressants
(sexual dysfunction induced by; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT Analgesics
(sexual pain disorders; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1, antagonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2, antagonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT Adrenoceptor antagonists
(α-; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT 57576-52-0, Thromboxane A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT 58-22-0, Testosterone
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and replacement agents; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT 50-28-2, Estradiol, biological studies 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT 57-83-0, Progesterone, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)
IT 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P 425638-96-6P
425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P 425639-07-2P
425639-10-7P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P
425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 425639-35-6P
425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P 425639-45-8P
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425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P 425639-65-2P
425639-68-5P 425639-70-9P 425639-72-1P 425639-74-3P 425639-76-5P
425639-77-6P 425639-79-8P 425639-81-2P 425639-83-4P 425639-85-6P
425639-87-8P 425639-89-0P 425639-91-4P 425639-93-6P 425639-95-8P
425639-96-9P 425639-97-0P 425639-98-1P 425639-99-2P 425640-00-2P

425640-01-3P 425640-02-4P 425640-03-5P 425640-15-9P 425640-23-9P
425641-28-7P 429657-44-3P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 50-50-0, Estradiol benzoate 102577-19-5, **Neuromedin** B
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 426213-31-2P 426213-32-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 58-18-4, Methyl testosterone 59-92-7, biological studies 71-58-9, Medroxyprogesterone acetate 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 28860-95-9, Carbidopa 37221-79-7, Vasoactive intestinal polypeptide 37221-79-7D, Vasoactive intestinal polypeptide, analogs 114798-26-4, Losartan 204066-72-8 204066-73-9 204066-75-1
204066-76-2 204066-78-4 204066-79-5 204066-80-8 204066-82-0
204066-83-1 204066-84-2 204066-86-4 204066-87-5 204066-89-7
204066-93-3 204066-95-5 204067-01-6 204067-38-9 215297-27-1
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425641-00-5 425641-01-6 425641-02-7 425641-03-8 425641-04-9
425641-05-0 425641-06-1 425641-07-2 425641-08-3 425641-09-4
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425641-20-9 425641-21-0 425641-22-1 425641-23-2 425641-24-3
425641-25-4 425641-26-5 425641-27-6 425641-29-8 425641-30-1
428864-38-4 428864-39-5 428864-40-8 428864-41-9 428864-42-0
428864-43-1 428864-44-2 428864-45-3 428864-46-4 428864-47-5
428864-48-6 428864-49-7 428864-50-0 428864-51-1 428864-52-2
428864-53-3 428864-54-4 428864-55-5 428864-56-6 428864-57-7
428864-58-8 428864-59-9 428864-63-5 428864-64-6 428864-66-8
428864-67-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 388630-36-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**bombesin** receptor antagonists, and combinations with other

agents, for treatment of sexual dysfunction)

IT 337962-74-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(**bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 128908-32-7, Melanocortin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 9000-81-1, Acetylcholinesterase 9025-82-5, Phosphodiesterase 9068-52-4, Phosphodiesterase V 82707-54-8, Neutral endopeptidase 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 9088-07-7, Natriuretic factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 25506-37-0P 31558-54-0P 63430-65-9P 73717-05-2P 97534-88-8P 97557-59-0P 105754-24-3P 137140-98-8P 158556-65-1P 158951-86-1P 159672-85-2P 159672-86-3P 160233-08-9P 172154-13-1P 172154-15-3P 172154-17-5P 172154-18-6P 204067-15-2P 204067-16-3P 204067-17-4P 291761-10-9P 337962-91-1P 388630-99-7P 425641-31-2P 425641-32-3P 425641-33-4P 425641-34-5P 425641-39-0P 425641-46-9P 425641-47-0P 425641-48-1P 425641-49-2P 425641-50-5P 425641-51-6P 425641-52-7P 425641-53-8P 428864-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; **bombesin** receptor antagonists, and combinations with other agents, for treatment of sexual dysfunction)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid 65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid 85-46-1, 1-Naphthalenesulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2 93-03-8 93-11-8, 2-Naphthalenesulfonyl chloride 93-25-4, (2-Methoxyphenyl)acetic acid 98-31-7 98-59-9 98-60-2 98-74-8 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0 99-94-5, 4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8, (4-Methoxyphenyl)acetic acid 104-03-0, (4-Nitrophenyl)acetic acid 105-13-5 108-86-1, Bromobenzene, reactions 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7 122-78-1, Benzeneacetaldehyde 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7 349-88-2 349-95-1 445-29-4, 2-Fluorobenzoic acid 446-51-5 451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid 527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid 552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions 579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid 587-03-1 589-18-4 591-17-3, 1-Bromo-3-methylbenzene 605-65-2 610-16-2, 2-Dimethylaminobenzoic acid 612-16-8 613-89-8 615-18-9, 2-Chlorobenzoxazole 619-25-0 619-73-8 621-36-3, m-Tolylacetic acid 621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid

644-36-0, o-Tolylacetic acid 673-06-3, D-Phenylalanine 701-27-9
776-04-5 777-44-6 873-76-7 874-97-5 877-65-6 879-65-2,
Quinoxaline-2-carboxylic acid 931-97-5, 1-Hydroxycyclohexanecarbonitrile
934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5,
1H-Indole-2-carboxylic acid 1592-38-7, 2-Naphthalenemethanol 1656-44-6
1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic
acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8 1805-32-9
1877-72-1, 3-Cyanobenzoic acid 1899-93-0 1918-79-2,
5-Methylthiophene-2-carboxylic acid 1939-99-7, Benzenemethanesulfonyl
chloride 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6,
[1,1'-Biphenyl]-2-sulfonyl chloride 2766-74-7 2888-06-4 2905-21-7
2905-23-9 2991-42-6 3405-77-4, 5-Methylisoxazole-3-carboxylic acid
3622-35-3, Benzothiazole-6-carboxylic acid 4052-30-6,
4-Methanesulfonylbenzoic acid 4254-29-9 4265-16-1,
Benzofuran-2-carbaldehyde 4533-95-3 4533-96-4 4780-79-4,
1-Naphthalenemethanol 5345-27-7 6314-28-9, Benzo[b]thiophene-2-
carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2,
3-Thiopheneacetic acid 6973-60-0 7693-46-1, p-Nitrophenyl
chloroformate 10130-74-2 10333-68-3, 2-Pyrrol-1-ylbenzoic acid
13826-35-2 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole 15084-51-2
16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9,
2-Thiophenesulfonyl chloride 16709-25-4 17078-28-3,
(4-Dimethylaminophenyl)acetic acid 17849-38-6 18704-37-5,
8-Quinolinesulfonyl chloride 23095-31-0 23806-24-8,
3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-
carboxylic acid 24424-99-5, Di-tert-butyl dicarbonate 24974-75-2
26638-43-7 28286-86-4 38594-42-2 39774-26-0, 2-Bromo-6-
phenylpyridine 42413-03-6 49584-26-1 51527-73-2 54997-92-1
56542-67-7 56946-83-9 59337-92-7 69360-26-5 71648-21-0
73713-79-8 80466-79-1 82964-91-8 88398-93-0 91170-93-3
94108-56-2 99924-18-2 100516-88-9, 6-Quinolinemethanol 114322-14-4,
2,1,3-Benzoxadiazole-4-sulfonyl chloride 118783-85-0 137049-00-4
137049-02-6 142854-50-0 151858-64-9 160233-27-2 166964-37-0
185908-35-4 204067-08-3 204067-12-9 206262-15-9 206262-83-1
216394-05-7 216394-11-5 425641-35-6 425641-36-7 425641-37-8
425641-38-9 425641-40-3 425641-41-4 425641-42-5 425641-43-6
425641-45-8 426213-33-4 426213-34-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **bombesin** receptor antagonists, and combinations
with other agents, for treatment of sexual dysfunction)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sensitizing agents; **bombesin** receptor antagonists, and
combinations with other agents, for treatment of sexual dysfunction)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrates; **bombesin** receptor antagonists, and combinations
with other agents, for treatment of sexual dysfunction)

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
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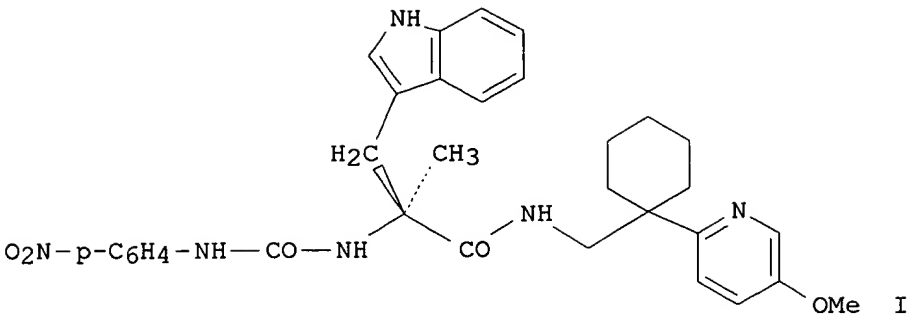

I

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compds., for example PDE5 inhibitors, NEP inhibitors and lasofoxifene. Preparation of **bombesin** receptor antagonists consisting of α-Me tryptophane (e.g., I) or α-methylphenylalanine derivs. was given. In tests on sexually-dysfunctional male rats, it was concluded that I had a stimulatory effect, at the level of sexual desire, performance, and **anorgasmy**. In tests on sexually-dysfunctional female rats, it was concluded that I had a stimulatory effect on proceptivity, which was unaffected by repeated administration.

ACCESSION NUMBER: 2002:869567 CAPLUS
DOCUMENT NUMBER: 137:370356
TITLE: Preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females
INVENTOR(S): Gonzalez, Maria Isabel; Higginbottom, Michael; Stock, Herman Thijs; Pritchard, Martyn Clive; Pinnock, Robert Denham; Van der Graaf, Pieter Hadewijn; Naylor, Alisdair Mark; Wayman, Christopher Peter
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 105 pp., Cont.-in-part of U.S. Pat. Appl. 2002 58,606.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169101	A1	20021114	US 2001-999284	20011115
US 2002058606	A1	20020516	US 2001-759777	20010112

PRIORITY APPLN. INFO.:

US 1999-133355P	P	19990510
WO 2000-GB1787	W	20000510
US 2000-700165	A2	20001109
US 2001-759777	A2	20010112
GB 2001-9910	A	20010423
GB 2001-11037	A	20010504

OTHER SOURCE(S): MARPAT 137:370356
TI Preparation and use of **bombesin** receptor antagonists for

treatment of sexual dysfunction in males and females

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females. They may be selective BB1 antagonists or mixed BB1/BB2 antagonists. Combinations are disclosed of **bombesin** receptor antagonists with a range of other active compds., for example PDE5 inhibitors, NEP inhibitors and lasofoxifene. Preparation of **bombesin** receptor antagonists consisting of α-Me tryptophane (e.g., I) or α-methylphenylalanine derivs. was given. In tests on sexually-dysfunctional male rats, it was concluded that I had a stimulatory effect, at the level of sexual desire, performance, and **anorgasmy**. In tests on sexually-dysfunctional female rats, it was concluded that I had a stimulatory effect on proceptivity, which was unaffected by repeated administration.

ST **bombesin** receptor antagonist amino acid prepn sexual dysfunction

IT Behavior
(arousal; preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT Sexual behavior
(disorder; preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT Human
(preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT **Bombesin** receptors
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT Drugs
(sexual dysfunction induced by; preparation and use of **bombesin** receptor antagonists for treatment of sexual dysfunction in males and females)

IT 105754-24-3P 204067-15-2P 204067-16-3P 204067-17-4P 337962-91-1P
388630-83-9P 425641-31-2P 425641-32-3P 425641-34-5P 425641-40-3P
425641-41-4P 425641-42-5P 425641-43-6P 425641-45-8P 425641-46-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of in the preparation of **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 337962-93-3P 425638-88-6P 425638-90-0P 425638-92-2P 425638-94-4P
425638-96-6P 425638-98-8P 425639-00-5P 425639-02-7P 425639-04-9P
425639-07-2P 425639-13-0P 425639-16-3P 425639-19-6P 425639-22-1P
425639-25-4P 425639-28-7P 425639-31-2P 425639-33-4P 425639-35-6P
425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P 425639-45-8P
425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P 425639-52-7P
425639-53-8P 425639-55-0P 425639-57-2P 425639-59-4P 425639-61-8P
425639-63-0P 425639-65-2P 425639-68-5P 425639-70-9P 425639-72-1P
425639-74-3P 425639-76-5P 425639-77-6P 425639-79-8P 425639-81-2P
425639-83-4P 425639-85-6P 425639-87-8P 425639-89-0P 425639-91-4P
425639-93-6P 425639-95-8P 425639-96-9P 425639-97-0P 425639-98-1P
425639-99-2P 425640-00-2P 425640-01-3P 425640-02-4P 425640-03-5P

425640-04-6P 425640-06-8P 425640-08-0P 425640-09-1P 425640-10-4P
425640-11-5P 425640-12-6P 425640-14-8P 425640-15-9P 425640-17-1P
425640-18-2P 425640-20-6P 425640-21-7P 425640-23-9P 425640-24-0P
425640-26-2P 425640-28-4P 425640-30-8P 425640-32-0P 425640-34-2P
425640-36-4P 425640-38-6P 425640-39-7P 425640-40-0P 425640-41-1P
425640-43-3P 425640-45-5P 425640-47-7P 425640-49-9P 425640-51-3P
425640-53-5P 425640-55-7P 425640-57-9P 425640-59-1P 425640-60-4P
425640-62-6P 425640-64-8P 425640-66-0P 425640-68-2P 425640-70-6P
425640-72-8P 425640-74-0P 425640-76-2P 425640-78-4P 425640-80-8P
425640-82-0P 425640-83-1P 425640-84-2P 425640-85-3P 425640-86-4P
425640-87-5P 425640-88-6P 425640-89-7P 425640-90-0P 425640-91-1P
425640-92-2P 425640-93-3P 425640-94-4P 425640-95-5P 425640-96-6P
425640-97-7P 425640-98-8P 425640-99-9P 425641-00-5P 425641-01-6P
425641-02-7P 425641-03-8P 425641-04-9P 425641-05-0P 425641-06-1P
425641-07-2P 425641-08-3P 425641-09-4P 425641-10-7P 425641-11-8P
425641-12-9P 425641-13-0P 425641-14-1P 425641-15-2P 425641-16-3P
425641-17-4P 425641-18-5P 425641-19-6P 425641-20-9P 425641-21-0P
425641-22-1P 425641-23-2P 425641-24-3P 425641-25-4P 425641-26-5P
425641-27-6P 425641-28-7P 425641-29-8P 425641-30-1P 425641-39-0P
426213-31-2P 426213-32-3P 426267-06-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of as **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 204067-01-6 428864-38-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of as **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 337962-74-0P 388630-36-2P
RL: PUR (Purification or recovery); PREP (Preparation)
(preparation of as **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 425641-33-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of as **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 187609-88-7 204066-72-8 204066-73-9 204066-75-1 204066-76-2
204066-78-4 204066-79-5 204066-80-8 204066-82-0 204066-83-1
204066-84-2 204066-86-4 204066-89-7 204066-95-5 204067-38-9
425639-10-7 428864-39-5 428864-40-8 428864-41-9 428864-42-0
428864-43-1 428864-45-3 428864-47-5 428864-48-6 428864-49-7
428864-50-0 428864-51-1 428864-52-2 428864-53-3 428864-54-4
428864-55-5 428864-56-6 428864-57-7 428864-58-8 428864-59-9
428864-63-5 428864-64-6 428864-66-8 428864-67-9 429657-44-3
475247-11-1 475247-13-3 475247-25-7 475249-13-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of as **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid 65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid 85-46-1, Naphthalene-1-sulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2, o-Tolylmethanol 93-03-8, (3,4-Dimethoxyphenyl)methanol 93-11-8, Naphthalene-2-sulfonyl chloride 93-25-4, (2-

Methoxyphenyl)acetic acid 98-31-7, 3,4-Dichlorobenzenesulfonyl chloride 98-59-9, 4-Methylbenzenesulfonyl chloride 98-60-2, 4-Chlorobenzenesulfonyl chloride 98-74-8, 4-Nitrobenzenesulfonyl chloride 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-81-0, 2-Bromo-1-(4-nitrophenyl)-ethanone 99-94-5, 4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8, (4-Methoxyphenyl)acetic acid 105-13-5, (4-Methoxyphenyl)methanol 108-86-1, Bromobenzene, reactions 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7, 3-Nitrobenzenesulfonyl chloride 122-78-1, Phenylacetaldehyde 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7, (3-Trifluoromethylphenyl)methanol 349-88-2, 4-Fluorobenzenesulfonyl chloride 349-95-1, (4-Trifluoromethylphenyl)methanol 445-29-4, 2-Fluorobenzoic acid 446-51-5, (2-Fluorophenyl)methanol 451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid 527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid 552-16-9, 2-Nitrobenzoic acid 555-16-8, 4-Nitrobenzaldehyde, reactions 579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid 587-03-1, m-Tolylmethanol 589-18-4, p-Tolylmethanol 591-17-3, 1-Bromo-3-methylbenzene 605-65-2, 5-DimethylaminoNaphthalene-1-sulfonyl chloride 610-16-2, 2-Dimethylaminobenzoic acid 612-16-8, (2-Methoxyphenyl)methanol 613-89-8, 2-Amino-1-phenylethanone 615-18-9, 2-Chlorobenzoxazole 619-25-0, (3-Nitrophenyl)methanol 619-73-8, (4-Nitrophenyl)methanol 621-36-3, m-Tolylacetic acid 621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid 644-36-0, o-Tolylacetic acid 673-06-3, D-Phenylalanine 701-27-9, 3-Fluorobenzenesulfonyl chloride 776-04-5, 2-Trifluoromethylbenzenesulfonyl chloride 777-44-6, 3-Trifluoromethylbenzenesulfonyl chloride 873-76-7, (4-Chlorophenyl)methanol 874-97-5, 3-Hydroxymethylbenzonitrile 877-65-6, (4-tert-Butylphenyl)methanol 879-65-2, Quinoxaline-2-carboxylic acid 931-97-5, 1-Hydroxycyclohexanecarbonitrile 934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5, 1H-Indole-2-carboxylic acid 1532-97-4, 4-Bromoisoquinoline 1592-38-7, Naphthalen-2-ylmethanol 1656-44-6, 2,4-Dinitrobenzenesulfonyl chloride 1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8, (2,4-Dichlorophenyl)methanol 1805-32-9, (3,4-Dichlorophenyl)methanol 1877-72-1, 3-Cyanobenzoic acid 1899-93-0, 3-Methylbenzenesulfonyl chloride 1918-79-2, 5-Methylthiophene-2-carboxylic acid 1939-99-7, Phenylmethanesulfonyl chloride 2052-07-5, 2-Bromobiphenyl 2104-06-5 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6, Biphenyl-2-sulfonyl chloride 2766-74-7, 5-Chlorothiophene-2-sulfonyl chloride 2888-06-4, 3-Chlorobenzenesulfonyl chloride 2905-21-7, 2-Fluorobenzenesulfonyl chloride 2905-23-9, 2-Chlorobenzenesulfonyl chloride 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3405-77-4, 5-Methylisoxazole-3-carboxylic acid 3622-35-3, Benzothiazole-6-carboxylic acid 3740-52-1, (2-Nitrophenyl)acetic acid 4052-30-6, 4-Methanesulfonylbenzoic acid 4254-29-9, Indan-2-ol 4265-16-1, Benzofuran-2-carbaldehyde 4533-95-3, 2-Chloro-5-nitrobenzenesulfonyl chloride 4533-96-4, 4-Chloro-2-nitrobenzenesulfonyl chloride 4595-59-9, 5-Bromopyrimidine 4780-79-4, Naphthalen-1-ylmethanol 5345-27-7, 3-Methanesulfonylbenzoic acid 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2, Thiophen-3-ylacetic acid 6973-60-0, 1-Methyl-1H-pyrrole-2-carboxylic acid 7693-46-1, 4-Nitrophenylchloroformate 10130-74-2, 3-Methoxybenzenesulfonyl chloride 10333-68-3, 2-Pyrrol-1-ylbenzoic acid 13826-35-2, (3-Phenoxyphenyl)methanol 15084-51-2, 4-tert-

Butylbenzenesulfonyl chloride 16136-58-6, 1-Methyl-1H-Indole-2-carboxylic acid 16629-19-9, Thiophene-2-sulfonyl chloride 16709-25-4 17078-28-3, (4-Dimethylaminophenyl)acetic acid 17849-38-6, (2-Chlorophenyl)methanol 18704-37-5, Quinoline-8-sulfonyl chloride 19524-06-2, 4-Bromopyridine hydrochloride 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-carboxylic acid 24974-75-2, (2-Nitrophenyl)methanesulfonyl chloride 25952-53-8, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride 26638-43-7, 2-Chlorosulfonylbenzoic acid methyl ester 28286-86-4, 2,4-Dichloro-5-methylbenzenesulfonyl chloride 28385-45-7 38594-42-2, (2,3-Dichlorophenyl)methanol 39774-26-0, 2-Bromo-6-phenylpyridine 42413-03-6, 3-Chloro-4-methylbenzenesulfonyl chloride 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51527-73-2, 2,4,6-Trichlorobenzenesulfonyl chloride 54997-92-1, 4-Butylbenzenesulfonyl chloride 56542-67-7, 3-Cyanobenzenesulfonyl chloride 56946-83-9, 2,5-Dichlorothiophene-3-sulfonyl chloride 59337-92-7, 3-Chlorosulfonylthiophene-2-carboxylic acid, methyl ester 69360-26-5, 2-Cyanobenzenesulfonyl chloride 71648-21-0, (3-Ethoxyphenyl)methanol 73713-79-8 80466-79-1, 3,5-Dimethylisoxazole-4-sulfonyl chloride 82964-91-8, 4-Methanesulfonylbenzenesulfonyl chloride 88398-93-0, 5-Chloro-1,3-dimethyl-1H-pyrazole-4-sulfonyl chloride 91170-93-3, 3-Chloro-4-fluorobenzensulfonyl chloride 94108-56-2, 4-Trifluoromethoxybenzenesulfonyl chloride 99924-18-2, 5-Phenyloxazole-4-carboxylic acid 100516-88-9, Quinolin-6-ylmethanol 114322-14-4, Benzo[c]1,2,5-oxadiazole-4-sulfonyl chloride 118783-85-0 137049-00-4, 1-Methyl-1H-imidazole-4-sulfonyl chloride 137049-02-6, 1,2-Dimethyl-1H-imidazole-4-sulfonyl chloride 142854-50-0 151858-64-9, 5-Pyridin-2-ylthiophene-2-sulfonyl chloride 160233-27-2, 5-Isoxazol-3-ylthiophene-2-sulfonyl chloride 166964-37-0, 5-Benzenesulfonylthiophene-2-sulfonyl chloride 185908-35-4, 8-Nitronaphthalene-1-sulfonyl chloride 204067-12-9 206262-15-9, 2-p-Tolyloxybenzenesulfonyl chloride 206262-83-1, 5-Methyl-2-phenoxybenzenesulfonyl chloride 216394-05-7, 5-Bromo-6-chloropyridine-3-sulfonyl chloride 216394-11-5, 2-Methoxy-4-methylbenzenesulfonyl chloride 425641-36-7 425641-37-8 425641-38-9 425641-47-0 426213-33-4 426213-34-5 475250-18-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the preparation of **bombesin** receptor antagonists for treatment of sexual dysfunction)

IT 180916-16-9, Lasofoxifene
RL: MSC (Miscellaneous)
(treatment of sexual dysfunction with **bombesin** receptor antagonists and)

L4 ANSWER 7 OF 15 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 3

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females.

CLMN 23 21 Figure(s).
FIG. 1: Effect of (S) 3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexyl-methyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)propionamide (Compound (1)) on female rat sexual proceptivity.
FIG. 2: Effect of Compound (1) on female rat sexual receptivity.
FIG. 3: Effect of repeated administration of Compound (1) on female rat proceptivity.
FIG. 4: Effect of intracerebroventricular administration of Compound (1) on female rat sexual proceptivity.

FIG. 5: Inhibitory effect of NMB on female rat sexual proceptivity and antagonism of this effect by Compound (1).
FIG. 6: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through progesterone.
FIG. 7: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through oestradiol.
FIG. 8: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through prolactin.
FIG. 9: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through LH.
FIG. 10: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through FSH.
FIG. 11: Effect of Compound (1) on the sexual behaviour of normal male rats (Mount Latency).
FIG. 12: Effect of Compound (1) on the sexual behaviour of normal male rats (Intromission Latency).
FIG. 13: Effect of Compound (1) on the sexual behaviour of normal male rats (Number of Mounts+Intromission).
FIG. 14: Effect of Compound (1) on the sexual behaviour of normal male rats (Ejaculation Latency).
FIG. 15: Effect of Compound (1) on the sexual behaviour of normal male rats (Refractory Period).
FIG. 16: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (Mount Latency).
FIG. 17: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (Ejaculation Latency).
FIG. 18: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (% animals ejaculating).
FIG. 19: Effect of (S)-3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2ylamino)-propionamide (Compound (2)) in PEG 200 on female rat sexual proceptivity.
FIG. 20: Effect of Compound (2) in methylcellulose on female rat sexual proceptivity.
FIG. 21: Effect of Compound (2) in PEG 200 on female rat sexual receptivity.

AN	10114999 IFIPAT;IFIUDB;IFICDB
TITLE:	TREATMENT OF SEXUAL DYSFUNCTION; ADMINISTERING A **BOMBESIN** RECEPTOR ANTAGONIST.
INVENTOR(S):	Gonzalez; Maria Isabel, Cambridge, GB Pinnock; Robert Denham, Cambridge, GB Pritchard; Martyn Clive, Huntingdon, GB
PATENT ASSIGNEE(S):	Unassigned
AGENT:	Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, MI, 48105, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2002058606	A1	20020516
APPLICATION INFORMATION:	US 2001-759777		20010112

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION-IN-PART OF:	US 2000-700165	20001109	PENDING

	NUMBER	DATE

DELACROIX

PRIORITY APPLN. INFO.: US 1999-133355P 19990510 (Provisional)
FAMILY INFORMATION: US 2002058606 20020516
DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION
OTHER SOURCE: CA 136:372081
NUMBER OF CLAIMS: 23 21 Figure(s).
DESCRIPTION OF FIGURES:
FIG. 1: Effect of (S) 3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexyl-methyl)-2-methyl-2-(3-(4-nitro-phenyl)-ureido)propionamide (Compound (1)) on female rat sexual proceptivity.
FIG. 2: Effect of Compound (1) on female rat sexual receptivity.
FIG. 3: Effect of repeated administration of Compound (1) on female rat proceptivity.
FIG. 4: Effect of intracerebroventricular administration of Compound (1) on female rat sexual proceptivity.
FIG. 5: Inhibitory effect of NMB on female rat sexual proceptivity and antagonism of this effect by Compound (1).
FIG. 6: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through progesterone.
FIG. 7: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through oestradiol.
FIG. 8: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through prolactin.
FIG. 9: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through LH.
FIG. 10: Results of an investigation to show whether the effect of Compound (1) on female sexual behaviour is mediated through FSH.
FIG. 11: Effect of Compound (1) on the sexual behaviour of normal male rats (Mount Latency).
FIG. 12: Effect of Compound (1) on the sexual behaviour of normal male rats (Intromission Latency).
FIG. 13: Effect of Compound (1) on the sexual behaviour of normal male rats (Number of Mounts+Intromission).
FIG. 14: Effect of Compound (1) on the sexual behaviour of normal male rats (Ejaculation Latency).
FIG. 15: Effect of Compound (1) on the sexual behaviour of normal male rats (Refractory Period).
FIG. 16: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (Mount Latency).
FIG. 17: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (Ejaculation Latency).
FIG. 18: Effect of Compound (1) on the sexual behaviour of sexually dysfunctional male rats (% animals ejaculating).
FIG. 19: Effect of (S)-3-(1H-Indol-3-yl)-N-(1-(5-methoxy-pyridin2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2ylamino)-propionamide (Compound (2)) in PEG 200 on female rat sexual proceptivity.
FIG. 20: Effect of Compound (2) in methylcellulose on female rat sexual proceptivity.
FIG. 21: Effect of Compound (2) in PEG 200 on female rat sexual receptivity.

TI TREATMENT OF SEXUAL DYSFUNCTION; ADMINISTERING A **BOMBESIN** RECEPTOR ANTAGONIST.

AB **Bombesin** receptor antagonists have been found to be useful in the treatment of sexual dysfunction in both males and females.

ECLM . . . sexual dysfunction which comprises administering to a subject suffering therefrom and in need of treatment an effective amount of a

bombesin receptor antagonist.

ACLM . . . sexual dysfunction which comprises administering to a subject suffering therefrom and in need of treatment an effective amount of a **bombesin** receptor antagonist.

. . . method of claim 1, wherein the dysfunction is associated with hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or **anorgasmy**, or sexual pain disorders.

7. The method of claim 1, wherein the **bombesin** receptor antagonist has a preferential affinity for the BB1 receptor.

8. The method of claim 1, wherein there is administered to the subject an effective amount of a non-peptide **bombesin** receptor antagonist.

9. The method of claim 8, wherein the non-peptide **bombesin** receptor antagonist is a compound that is absorbable when administered orally.

10. The method of claim 1, wherein there is administered to the subject an effective amount of a **bombesin** receptor antagonist which is a peptide.

11. The method of claim 1, which comprises administering to a subject a **bombesin** receptor antagonist in combination with a vasodilator useful for the treatment of sexual dysfunction.

17. The method of claim 1, which comprises administering to a subject a **bombesin** receptor antagonist in combination with a modulator of steroid hormones, a steroid hormone or a hormone product useful for the. . .

19. The method of claim 1, which comprises administering to a subject a **bombesin** receptor antagonist in combination with a neurotransmitter agonist or antagonist, a monoamine synthesis modifier, or a monoamine metabolism or uptake. . .

21. The method of claim 11 wherein the **bombesin** receptor antagonist and the vasodilator are simultaneously administered to the subject in the form of a composition containing a unit dose of the **bombesin** receptor antagonist, a unit dose of the vasodilator and a pharmaceutically acceptable carrier or diluent.

22. The method of claim 17 wherein the **bombesin** receptor antagonist and the modulator of steroid hormones, steroid hormone or hormone product are simultaneously administered to the subject in the form of a composition containing a unit dose of the **bombesin** receptor antagonist, a unit dose of the modulator of steroid hormones, steroid hormone or hormone product and a pharmaceutically acceptable. . .

23. The method of claim 19 wherein the **bombesin** receptor antagonist and the neurotransmitter agonist or antagonist, monoamine synthesis modifier, or monoamine metabolism or uptake modifier are simultaneously administered to the subject in the form of a composition containing a unit dose of the **bombesin** receptor antagonist, a unit dose of the neurotransmitter agonist or antagonist, monoamine synthesis modifier, or monoamine metabolism or uptake modifier. . .

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention is directed to B-superfamily conotoxin peptides, derivs. or pharmaceutically acceptable salts thereof. The present invention is further directed to the use of this peptide, derivs. thereof and pharmaceutically acceptable salts thereof for the treatment of disorders associated with voltage-gated ion channels, ligand-gated channels, and other receptors. The invention is further directed to the nucleic acid sequences encoding the B-superfamily conotoxin peptides and encoding B-superfamily conotoxin propeptides, as well as the B-superfamily

conotoxin propeptides. Thus, the DNA encoding 75 novel preprotoxins of various Conus species and the encoded conotoxins are disclosed. Truncated forms of these conotoxins inhibited growth of human breast and pancreatic adenocarcinoma cells in culture. The binding of these truncated conotoxins to somatostation and melanocortin receptors was analyzed.

ACCESSION NUMBER: 2002:594869 CAPLUS
DOCUMENT NUMBER: 137:164897
TITLE: B-superfamily conotoxins and cDNAs and their use in pharmaceuticals and in drug screening
INVENTOR(S): Jones, Robert M.; Olivera, Baldomero M.; Watkins, Maren; Garrett, James E.
PATENT ASSIGNEE(S): Cognetix, Inc., USA; University of Utah Research Foundation
SOURCE: PCT Int. Appl., 230 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060923	A2	20020808	WO 2002-US2523	20020129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003170222	A1	20030911	US 2002-58053	20020129

PRIORITY APPLN. INFO.: US 2001-264323P P 20010129

IT **Gastrin-releasing peptide** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (disorders of; b-superfamily conotoxins and cDNAs and their use in pharmaceuticals and in drug screening)

IT Sexual behavior
(**impotence**; b-superfamily conotoxins and cDNAs and their use in pharmaceuticals and in drug screening)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**neuromedin**, disorders of; b-superfamily conotoxins and cDNAs and their use in pharmaceuticals and in drug screening)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (type BB2, disorders of; b-superfamily conotoxins and cDNAs and their use in pharmaceuticals and in drug screening)

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AB The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 receptor, which inhibitor is selective for an NPY or NPY Y1 receptor associated with male genitalia, in the preparation/manufacture of a medicament for the treatment or prevention of male erectile dysfunction (MED).

ACCESSION NUMBER: 2002:465801 CAPLUS

DOCUMENT NUMBER: 137:52344
TITLE: Treatment of male sexual dysfunction
INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047670	A1	20020620	WO 2001-IB2399	20011210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002028799	A1	20020307	US 2001-895367	20010629
US 2002102707	A1	20020801	US 2001-905846	20010713
AU 2002020977	A5	20020624	AU 2002-20977	~~20011210~~
EP 1347750	A1	20031001	EP 2001-270206	20011210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:

GB 2000-30647	A	20001215
GB 2001-8730	A	20010406
GB 2001-9910	A	20010423
GB 2001-11037	A	20010504
US 2001-895367	A	20010629
US 2001-905846	A	20010713
GB 2001-20679	A	20010824
GB 2000-16684	A	20000706
GB 2000-17387	A	20000714
US 2000-219100P	P	20000718
US 2000-220908P	P	20000726
US 2001-265358P	P	20010131
GB 2001-6167	A	20010313
GB 2001-8483	A	20010404
WO 2001-IB2399	W	20011210

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Bombesin** receptors
Endothelin receptors
Gastrin-releasing peptide receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT Sexual behavior
(**impotence**; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

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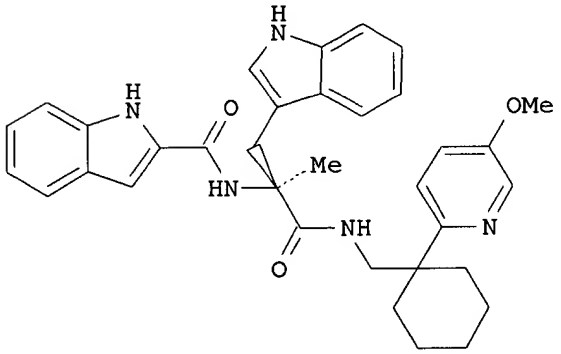
IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB3, antagonists; neuropeptide Y inhibitors for treatment of male sexual dysfunction)

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
GI



II

AB This invention discloses the preparation of title compds. Ar-(CH2)k-X-NR3-CR5(CH2Ar1)-CO-NR4-(CH2)l-(CR1R6)m-(CH2)n-R2 (I) and their pharmaceutically acceptable salts as **bombesin** receptor antagonists [wherein: k = 0, 1, 2; l = 0, 1, 2, 3; m = 0, 1; n = 0, 1, 2; X = CO, OCO, SO, SO2; Ar = (un)substituted benzimidazolyl, benzofuryl, indanyl, indolyl, naphthyl, Ph, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl, thiazolyl, etc.; Ar1 = groups given for Ar, plus pyridyl N-oxide; R1 = H, alkyl, (oxa- or aza)cycloalkyl; R2 = groups given for Ar, H, OH, alkoxy, NMe2, CONR12R13, certain substituted rings; R3-R5 = H, alkyl; R6 = H, Me, or together with R1 forms carbonyl or a C3-7 ring which can contain an oxygen or nitrogen atom; provided that when X = OCO, then l = 1-3 and m = 1]. Approx. 140 specific examples of I were prepared and/or claimed. For example, HBTU-mediated coupling of 1H-indole-2-carboxylic acid with the corresponding intermediate amine provided the claimed α-methyltryptophan amide II in 60% yield. In binding studies to cloned human BB1 and BB2 **bombesin** receptor subtypes, compound II had IC50 values of 11 nM and 119 nM, resp.

ACCESSION NUMBER: 2002:391703 CAPLUS
DOCUMENT NUMBER: 136:402022
TITLE: Preparation of (S)-α-methyltryptophan amide derivatives as **bombesin** receptor antagonists
INVENTOR(S): Higginbottom, Michael; Pritchard, Martin Clive; Stock,

Herman Thijs
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040469	A1	20020523	WO 2001-EP14401	20011116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2369117	A1	20020522	GB 2000-28104	20001117
AU 2002016079	A5	20020527	AU 2002-16079	20011116
EP 1334100	A1	20030813	EP 2001-996536	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015414	A	20030909	BR 2001-15414	20011116

PRIORITY APPLN. INFO.: GB 2000-28104 A 20001117
WO 2001-EP14401 W 20011116

OTHER SOURCE(S): CASREACT 136:402022; MARPAT 136:402022
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of (S)-α-methyltryptophan amide derivatives as **bombesin** receptor antagonists

AB This invention discloses the preparation of title compds. Ar-(CH2)k-X-NR3-CR5(CH2Ar1)-CO-NR4-(CH2)l-(CR1R6)m-(CH2)n-R2 (I) and their pharmaceutically acceptable salts as **bombesin** receptor antagonists [wherein: k = 0, 1, 2; l = 0, 1, 2, 3; m = 0, 1; n = 0, 1, 2; X = CO, OCO, SO, SO2; Ar = (un)substituted benzimidazolyl, benzofuryl, indanyl, indolyl, naphthyl, Ph, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl, thiazolyl, etc.; Ar1 = groups given for Ar, plus pyridyl N-oxide; R1 = H, alkyl, (oxa- or aza)cycloalkyl; R2 = groups given for Ar, H, OH, alkoxy, NMe2, CONR12R13, certain substituted rings; R3-R5 = H, alkyl; R6 = H, Me, or together with R1 forms carbonyl or a C3-7 ring which can contain an oxygen or nitrogen atom; provided that when X = OCO, then l = 1-3 and m = 1]. Approx. 140 specific examples of I were prepared and/or claimed. For example, HBTU-mediated coupling of 1H-indole-2-carboxylic acid with the corresponding intermediate amine provided the claimed α-methyltryptophan amide II in 60% yield. In binding studies to cloned human BB1 and BB2 **bombesin** receptor subtypes, compound II had IC50 values of 11 nM and 119 nM, resp.

ST **bombesin** receptor antagonist peptide analog methyltryptophan deriv prepn; sexual dysfunction treatment **bombesin** receptor antagonist tryptophan methyl prepn

IT Intestine, disease
(Crohn's, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT Mental disorder
(affective, seasonal, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analogs, (S)-α-methyltryptophan-containing; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Intestine, disease
(colitis, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Sexual behavior
(disorder, **anorgasmia**, female, treatment; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Sexual behavior
(disorder, male and female, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Appetite
Sleep
(disorder, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Porphyria
(hepatic; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Intestine, disease
(inflammatory, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Pancreas, neoplasm
(inhibitors, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Antitumor agents
(pancreas, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Anxiety
(panic disorder, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Mental disorder
(phobia, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT Analgesics
Antidepressants
Antiemetics
Antipsychotics
Antitumor agents
Anxiolytics
Cognition enhancers
Human
Lung, disease
(preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)
IT **Bombesin** receptors
Gastrin-releasing peptide receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT Hypertension
(pulmonary, treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT Anorexia
Digestive tract, disease
Prostate gland, neoplasm
Pruritus
(treatment of; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB1; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT **Bombesin** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type BB2; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT 80043-53-4, **Gastrin-releasing peptide**
102577-19-5, **Neuromedin**-b
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT 425639-35-6P 425639-37-8P 425639-39-0P 425639-41-4P 425639-43-6P
425639-45-8P 425639-47-0P 425639-48-1P 425639-49-2P 425639-50-5P
425639-52-7P 425639-53-8P 425639-55-0P 425639-57-2P 425639-59-4P
425639-61-8P 425639-63-0P 425639-65-2P 425639-68-5P 425639-70-9P
425639-72-1P 425639-74-3P 425639-76-5P 425639-77-6P 425639-79-8P
425639-83-4P 425639-85-6P 425639-87-8P 425639-89-0P 425639-91-4P
425639-93-6P 425639-95-8P 425639-96-9P 425639-97-0P 425639-98-1P
425639-99-2P 425640-00-2P 425640-01-3P 425640-02-4P 425640-03-5P
425640-04-6P 425640-06-8P 425640-08-0P 425640-09-1P 425640-10-4P
425640-11-5P 425640-12-6P 425640-14-8P 425640-15-9P 425640-17-1P
425640-18-2P 425640-20-6P 425640-21-7P 425640-23-9P 425640-24-0P
425640-26-2P 425640-28-4P 425640-30-8P 425640-32-0P 425640-34-2P
425640-36-4P 425640-38-6P 425640-39-7P 425640-40-0P 425640-41-1P
425640-43-3P 425640-45-5P 425640-47-7P 425640-49-9P 425640-51-3P
425640-53-5P 425640-55-7P 425640-57-9P 425640-59-1P 425640-60-4P
425640-62-6P 425640-64-8P 425640-66-0P 425640-68-2P 425640-70-6P
425640-72-8P 425640-74-0P 425640-76-2P 425640-78-4P 425640-80-8P
425640-82-0P 425640-83-1P 425640-84-2P 425640-85-3P 425640-86-4P
425640-87-5P 425640-88-6P 425640-89-7P 425640-90-0P 425640-91-1P
425640-92-2P 425640-93-3P 425640-94-4P 425640-95-5P 425640-96-6P
425640-97-7P 425640-98-8P 425640-99-9P 425641-00-5P 425641-02-7P
425641-04-9P 425641-05-0P 425641-07-2P 425641-08-3P 425641-09-4P
425641-11-8P 425641-12-9P 425641-13-0P 425641-14-1P 425641-15-2P
425641-16-3P 425641-17-4P 425641-18-5P 425641-19-6P 425641-20-9P
425641-21-0P 425641-22-1P 425641-23-2P 425641-24-3P 425641-25-4P
425641-26-5P 425641-27-6P 425641-28-7P 425641-29-8P 425641-30-1P
428864-63-5P 428864-64-6P 428864-66-8P 428864-67-9P 428876-73-7P,
(S)-2-((Benzo[c]-1,2,5-thiadiazol-4-ylsulfonyl)amino)-3-(1H-indol-3-yl)-2-methyl-N-((1-(pyridin-2-yl)cyclohexyl)methyl)propanamide 428876-74-8P,
(S)-2-((Benzo[c]-1,2,5-oxadiazol-4-ylsulfonyl)amino)-3-(1H-indol-3-yl)-2-methyl-N-((1-(pyridin-2-yl)cyclohexyl)methyl)propanamide 428876-75-9P
428876-76-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT 25506-37-0P, (4-Methoxyphenyl)methyl 4-nitrophenyl carbonate 31558-54-0P, (3,4-Dimethoxyphenyl)methyl 4-nitrophenyl carbonate 63430-65-9P 73717-05-2P, (2-Chlorophenyl)methyl 4-nitrophenyl carbonate 97534-88-8P, (4-Chlorophenyl)methyl 4-nitrophenyl carbonate 97557-59-0P, (4-Toluene)methyl 4-nitrophenyl carbonate 137140-98-8P, (4-tert-Butylphenyl)methyl 4-nitrophenyl carbonate 149358-14-5P, Quinolin-6-ylmethyl 4-nitrophenyl carbonate 158556-65-1P, (4-Nitrophenyl)methyl 4-nitrophenyl carbonate 158951-86-1P, Naphthalen-2-yl-methyl 4-nitrophenyl carbonate 159672-85-2P, Indan-2-yl 4-nitrophenyl carbonate 159672-86-3P, (2-Fluorophenyl)methyl 4-nitrophenyl carbonate 160233-08-9P, (2-Methoxyphenyl)methyl 4-nitrophenyl carbonate 172154-13-1P, (4-Trifluoromethylphenyl)methyl 4-nitrophenyl carbonate 172154-15-3P 172154-17-5P, (2-Toluene)methyl 4-nitrophenyl carbonate 172154-18-6P, Naphthalene-1-ylmethyl 4-nitrophenyl carbonate 204067-16-3P 204067-17-4P 291761-10-9P, (3-Ethoxyphenyl)methyl 4-nitrophenyl carbonate 425641-46-9P 425641-47-0P 425641-48-1P, (3,4-Dichlorophenyl)methyl 4-nitrophenyl carbonate 425641-49-2P, (3-Nitrophenyl)methyl 4-nitrophenyl carbonate 425641-50-5P 425641-51-6P, (3-Phenoxyphenyl)methyl 4-nitrophenyl carbonate 425641-52-7P, (3-Trifluoromethylphenyl)methyl 4-nitrophenyl carbonate 425641-53-8P, (2,3-Dichlorophenyl)methyl 4-nitrophenyl carbonate 428876-77-1P 428876-78-2P 428876-79-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT 55-22-1, Isonicotinic acid, reactions 62-23-7, 4-Nitrobenzoic acid 65-85-0, Benzoic acid, reactions 74-11-3, 4-Chlorobenzoic acid 85-46-1, Naphthalene-1-sulfonyl chloride 86-59-9, Quinoline-8-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 88-14-2, Furan-2-carboxylic acid 89-95-2, o-Tolylmethanol 93-03-8, (3,4-Dimethoxyphenyl)methanol 93-11-8, Naphthalene-2-sulfonyl chloride 93-25-4, (2-Methoxyphenyl)acetic acid 98-31-7, 3,4-Dichlorobenzenesulfonyl chloride 98-59-9, 4-Methylbenzenesulfonyl chloride 98-60-2, 4-Chlorobenzenesulfonyl chloride 98-74-8, 4-Nitrobenzenesulfonyl chloride 98-98-6, Pyridine-2-carboxylic acid 99-04-7, 3-Methylbenzoic acid 99-64-9, 3-Dimethylaminobenzoic acid 99-94-5, 4-Methylbenzoic acid 100-09-4, 4-Methoxybenzoic acid 104-01-8, (4-Methoxyphenyl)acetic acid 105-13-5, (4-Methoxyphenyl)methanol 118-90-1, 2-Methylbenzoic acid 118-91-2, 2-Chlorobenzoic acid 121-51-7, 3-Nitrobenzenesulfonyl chloride 153-91-3 156-38-7, (4-Hydroxyphenyl)acetic acid 349-75-7, (3-Trifluoromethylphenyl)methanol 349-88-2, 4-Fluorobenzenesulfonyl chloride 349-95-1, (4-Trifluoromethylphenyl)methanol 445-29-4, 2-Fluorobenzoic acid 446-51-5, (2-Fluorophenyl)methanol 451-82-1, (2-Fluorophenyl)acetic acid 488-93-7, Furan-3-carboxylic acid 527-72-0, Thiophene-2-carboxylic acid 535-80-8, 3-Chlorobenzoic acid 552-16-9, 2-Nitrobenzoic acid 579-75-9, 2-Methoxybenzoic acid 586-38-9, 3-Methoxybenzoic acid 587-03-1, m-Tolylmethanol 589-18-4, p-Tolylmethanol 605-65-2, 5-Dimethylaminonaphthalene-1-sulfonyl chloride 610-16-2, 2-Dimethylaminobenzoic acid 612-16-8, (2-Methoxyphenyl)methanol 619-25-0, (3-Nitrophenyl)methanol 619-73-8, (4-Nitrophenyl)methanol 621-36-3, m-Tolylacetic acid 621-37-4, (3-Hydroxyphenyl)acetic acid 622-47-9, p-Tolylacetic acid 644-36-0,

o-Tolylacetic acid 701-27-9, 3-Fluorobenzenesulfonyl chloride 776-04-5, 2-Trifluoromethylbenzenesulfonyl chloride 777-44-6, 3-Trifluoromethylbenzenesulfonyl chloride 837-95-6, 2-Nitro-4-trifluoromethylbenzenesulfonyl chloride 873-76-7, (4-Chlorophenyl)methanol 874-97-5, 3-Hydroxymethylbenzonitrile 877-65-6, (4-tert-Butylphenyl)methanol 879-65-2, Quinoxaline-2-carboxylic acid 934-60-1, 6-Methylpyridine-2-carboxylic acid 1477-50-5, 1H-Indole-2-carboxylic acid 1592-38-7, Naphthalen-2-ylmethanol 1656-44-6, 2,4-Dinitrobenzenesulfonyl chloride 1670-81-1, 1H-Indole-5-carboxylic acid 1670-82-2, 1H-Indole-6-carboxylic acid 1670-83-3, 1H-Indole-7-carboxylic acid 1777-82-8, (2,4-Dichlorophenyl)methanol 1805-32-9, (3,4-Dichlorophenyl)methanol 1877-72-1, 3-Cyanobenzoic acid 1899-93-0, 3-Methylbenzenesulfonyl chloride 1918-79-2, 5-Methylthiophene-2-carboxylic acid 1939-99-7, Phenylmethanesulfonyl chloride 2124-55-2, 1H-Indole-4-carboxylic acid 2688-90-6, Biphenyl-2-sulfonyl chloride 2766-74-7, 5-Chlorothiophene-2-sulfonyl chloride 2888-06-4, 3-Chlorobenzenesulfonyl chloride 2905-21-7, 2-Fluorobenzenesulfonyl chloride 2905-23-9, 2-Chlorobenzenesulfonyl chloride 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3405-77-4, 5-Methyl-isoxazole-3-carboxylic acid 3622-35-3, Benzothiazole-6-carboxylic acid 3740-52-1, (2-Nitrophenyl)acetic acid 4052-30-6, 4-Methanesulfonylbenzoic acid 4254-29-9, Indan-2-ol 4533-95-3, 2-Chloro-5-nitrobenzenesulfonyl chloride 4533-96-4, 4-Chloro-2-nitrobenzenesulfonyl chloride 4780-79-4, Naphthalen-1-ylmethanol 5345-27-7, 3-Methanesulfonylbenzoic acid 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6624-49-3, Isoquinoline-3-carboxylic acid 6964-21-2, Thiophen-3-ylacetic acid 6973-60-0, 1-Methyl-1H-pyrrole-2-carboxylic acid 7693-46-1, 4-Nitrophenyl chloroformate 10130-74-2, 3-Methoxybenzenesulfonyl chloride 10333-68-3, 2-Pyrrol-1-ylbenzoic acid 13826-35-2, (3-Phenoxyphenyl)methanol 15084-51-2, 4-tert-Butylbenzenesulfonyl chloride 16136-58-6, 1-Methyl-1H-indole-2-carboxylic acid 16629-19-9, Thiophene-2-sulfonyl chloride 17078-28-3, (4-Dimethylaminophenyl)acetic acid 17849-38-6, (2-Chlorophenyl)methanol 18704-37-5, Quinoline-8-sulfonyl chloride 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 23806-24-8, 3-Methylthiophene-2-carboxylic acid 23814-12-2, 1H-Benzotriazole-5-carboxylic acid 24424-99-5 24974-75-2, (2-Nitrophenyl)methanesulfonyl chloride 26638-43-7, 2-Chlorosulfonylbenzoic acid methyl ester 28286-86-4, 2,4-Dichloro-5-methylbenzenesulfonyl chloride 38594-42-2, (2,3-Dichlorophenyl)methanol 42413-03-6, 3-Chloro-4-methylbenzenesulfonyl chloride 49584-26-1, 4-Cyanobenzenesulfonyl chloride 51527-73-2, 2,4,6-Trichlorobenzenesulfonyl chloride 54090-08-3, 2-Chloro-5-trifluoromethylbenzenesulfonyl chloride 54997-92-1, 4-Butyl-benzenesulfonyl chloride 56542-67-7, 3-Cyanobenzenesulfonyl chloride 56946-83-9, 2,5-Dichlorothiophene-3-sulfonyl chloride 59337-92-7, 3-Chlorosulfonylthiophene-2-carboxylic acid methyl ester 69360-26-5, 2-Cyanobenzenesulfonyl chloride 71648-21-0, (3-Ethoxyphenyl)methanol 73713-79-8, Benzo[c]-1,2,5-thiadiazole-4-sulfonyl chloride 80466-79-1, 3,5-Dimethylisoxazole-4-sulfonyl chloride 82964-91-8, 4-Methanesulfonylbenzenesulfonyl chloride 88398-93-0, 5-Chloro-1,3-dimethyl-1H-pyrazole-4-sulfonyl chloride 91170-93-3, 3-Chloro-4-fluorobenzenesulfonyl chloride 94108-56-2, 4-Trifluoromethoxybenzenesulfonyl chloride 99924-18-2, 5-Phenyloxazole-4-carboxylic acid 100516-88-9, Quinolin-6-ylmethanol 114322-14-4, Benzo[c]-1,2,5-oxadiazole-4-sulfonyl chloride 137049-00-4, 1-Methyl-1H-imidazole-4-sulfonyl chloride 137049-02-6,

1,2-Dimethyl-1H-imidazole-4-sulfonyl chloride 151858-64-9,
5-Pyridin-2-ylthiophene-2-sulfonyl chloride 160233-27-2,
5-Isoxazol-3-ylthiophene-2-sulfonyl chloride 166964-37-0,
5-Benzenesulfonylthiophene-2-sulfonyl chloride 185908-35-4,
8-Nitronaphthalene-1-sulfonyl chloride 204067-08-3 204067-12-9
206262-15-9, 2-p-Tolyloxybenzenesulfonyl chloride 206262-83-1,
5-Methyl-2-phenoxybenzenesulfonyl chloride 216394-05-7,
5-Bromo-6-chloropyridine-3-sulfonyl chloride 216394-11-5,
2-Methoxy-4-methylbenzenesulfonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

IT 204067-15-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant; preparation of α-methyltryptophan amide derivs. as **bombesin** receptor antagonists)

L4 ANSWER 11 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-454833 [48] WPIDS
CR 2002-489427 [52]; 2002-740638 [80]
AB WO 200240022 A UPAB: 20031112
NOVELTY - Treatment of sexual dysfunction involves administering a peptide or non-peptide **bombesin** receptor antagonist (A).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of (A) in the manufacture of medicament for preventing or treating male or female sexual dysfunction.
ACTIVITY - Vasotropic.
MECHANISM OF ACTION - **Bombesin** receptor antagonist; neuromotransmitter agonist; neuromotransmitter antagonist; modulator of steroid hormones; monoamine synthesis modifier; monoamine metabolism or uptake modifier.
USE - In the manufacture of medicament for treating male and female sexual dysfunction associated with hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders, **anorgasmy**, sexual pain disorders, generalized unresponsiveness, ageing-related decline in sexual arousability or drug-induced sexual dysfunction (all claimed).
ADVANTAGE - (A) has a preferential affinity for BB1 receptor, can exert a neuromodulatory effect on sexual behavior and is absorbable when administered orally.
Dwg.0/21

ACCESSION NUMBER: 2002-454833 [48] WPIDS
CROSS REFERENCE: 2002-489427 [52]; 2002-740638 [80]
DOC. NO. CPI: C2002-129392
TITLE: Use of **bombesin** antagonist e.g. PD-176252, for treatment of male and female sexual dysfunction e.g. associated with hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or **anorgasmy** or sexual pain disorders.
DERWENT CLASS: B04
INVENTOR(S): GONZALEZ, M I; HIGGINBOTTOM, M; PINNOCK, R D; PRITCHARD, M C; STOCK, H T
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO; (WARN) WARNER LAMBERT CO LLC
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2002040022 A1 20020523 (200248)* EN 151
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001014046 A 20020527 (200261)
EP 1333829 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
BR 2000017374 A 20030930 (200373)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002040022	A1	WO 2000-GB4380	20001117
AU 2001014046	A	WO 2000-GB4380	20001117
		AU 2001-14046	20001117
EP 1333829	A1	EP 2000-976165	20001117
		WO 2000-GB4380	20001117
BR 2000017374	A	BR 2000-17374	20001117
		WO 2000-GB4380	20001117

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001014046	A	Based on	WO 2002040022
EP 1333829	A1	Based on	WO 2002040022
BR 2000017374	A	Based on	WO 2002040022

PRIORITY APPLN. INFO: WO 2000-GB4380 20001117

TI Use of **bombesin** antagonist e.g. PD-176252, for treatment of male and female sexual dysfunction e.g. associated with hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or **anorgasmy** or sexual pain disorders.

AB WO 200240022 UPAB: 20031112
NOVELTY - Treatment of sexual dysfunction involves administering a peptide or non-peptide **bombesin** receptor antagonist (A).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of (A) in the manufacture of medicament for preventing or treating male or female sexual dysfunction.
ACTIVITY - Vasotropic.
MECHANISM OF ACTION - **Bombesin** receptor antagonist; neuromotransmitter agonist; neuromotransmitter antagonist; modulator of steroid hormones; monoamine synthesis modifier; monoamine metabolism or uptake modifier.
USE -. . . of medicament for treating male and female sexual dysfunction associated with hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders, **anorgasmy**, sexual pain disorders, generalized unresponsiveness, ageing-related decline in sexual arousability or drug-induced sexual dysfunction (all claimed).
ADVANTAGE - (A). . .

TT TT: **BOMBESIN** ANTAGONIST TREAT MALE FEMALE SEX DYSFUNCTION

ASSOCIATE SEX DISORDER SEX DISORDER DISORDER SEX PAIN DISORDER.

L4 ANSWER 12 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-593206 [64] WPIDS
AB GB 2369118 A UPAB: 20021007
NOVELTY - Synthetic peptides (I) are new.
DETAILED DESCRIPTION - Synthetic peptides of formula (I) and their salts (especially hydrochlorides, mesylates and sulfates) are new.
j = 0-2;
k = 0-1;
l = 0-3;
m = 0-1;
n = 0-2;
q = 0-1;
r = 0-1;
Ar = phenyl, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl or thiazolyl, (all optionally substituted by 1-3 acetyl, alkoxy, alkyl, amino, CN, halo, OH, nitro, sulfonamido, sulfonyl, CF3, OCF3, CO2H, CH2CN, SO2CF3, CH2CO2H or (CH2)sNR7R8);
s = 0-3;
R7, R8 = H, 1-6C alkyl; or
NR7R8 = 5-7 membered aliphatic ring optionally containing 1-2 O atoms;
R1 = H, 1-6C alkyl or 5-7C cycloalkyl (optionally containing 1-2 N or O atoms);
R6 = H or Me; or
R1+R6 = C(O) or 3-7 membered aliphatic ring optionally containing an O or N atom;
Ar1 = Ar, indolyl or pyridyl-N-oxide;
R3-R5 = H or lower alkyl;
R2 = Ar, H, OH, alkoxy, -NMe2, -CONR9R10, or a group of formula (i)-(v);
R9, R10 = H or 1-6C alkyl; or
NR9R10 = 5-7 membered aliphatic ring optionally containing 1-2 O or N atoms;
p = 0-2;
Ar2 = phenyl or pyridyl;
X = a divalent radical derived from indane, tetrahydronaphthalene, naphthalene, benzimidazole, benzotriazole, 1,3-benzoxazole, benzothiophene, benzofuran, 1,3-benzothiazole, tetrahydroquinoline, tetrahydroisoquinoline, quinoline, isoquinoline or quinoxaline (all optionally substituted in the phenyl ring by R11 and R12), oxazole, pyridine, pyrimidine, pyrazine, pyridazine, 1,3,5-triazine, imidazole, 1,2,4-triazole, pyrrole, tetrazole, thiophene, 1,2,4-thiadiazole, imidazolidine, 1,3-thiazoline, furan, 1,2-oxazoline, 1,2-oxazolidine, 1,1-dioxo-1,2-thiazolidine, pyrazoline, pyrazole, 1,2,4-oxadiazoline, 1,2-thiazoline, pyrrolidine, 1,3,4-oxazole, 1,2,4-oxazole or benzene (all N atoms optionally substituted by lower alkyl);
R11, R12 = H, halo, OH, alkoxy, acetyl, nitro, CN, amino, CF3 or (CH2)tNR13R14;
t = 0-1;
R13, R14 = H, 1-6C alkyl or 5-7C cycloalkyl containing up to 2 O or N atoms;
provided that when r = 0, Ar is replaced by H.
INDEPENDENT CLAIMS are also included for the preparation of (I).
ACTIVITY - Vasotropic; Tranquilizer; Anxiolytic; Antidepressant; Antipsychotic; Sedative; Nootropic; Hypotensive; Cytostatic; Hepatotropic;

Gastrointestinal; Antiulcer; Antiinflammatory; Antiemetic; Analgesic;Anabolic; Anorectic; Antipruritic.

Ovariectomized adult female Sprague Dawley rats (180-200 g) were housed in groups of 6 in a reversed lighting system of 12 hours light:dark. 2 weeks after ovariectomy they were used for sexual activity tests, They were tested using sexual stimuli: an intact sexually experienced male and a receptive female (ovariectomised, primed with 5 micro g estradiol benzoate dissolved in corn oil and injected subcutaneously 48 hours before the test and with 0.5 mg progesterone 4 hours before the test). Sexually naive test and control animals were used. (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-propionamide (Ia) (30-100 mg/kg) dose-dependently increased the difference in the % time spent investigating the male stimuli minus female stimuli, with a MED of 100 mg/kg. The effect of this dose was similar to that of progesterone.

MECHANISM OF ACTION - Bombesin (BB) receptor antagonists.

In BB1 and BB2 binding assays using CHO-K1 cells stably expressing cloned human decapeptide neuromedin B (NMB) (for BB1 assay) and gastrin releasing peptide GRP receptors (for BB2 assay), (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-propionamide (Ia) bound to NMB and GRP with Ki values of 4 and 24 nM, respectively.

USE - (I) Can be used for antagonizing the effects of neuromedin B and/or gastrin-releasing peptide at bombesin receptors, for treating sexual dysfunction which may be characterized by generalized unresponsiveness or age-related decline in sexual arousability in a male or female patient, or treating sexual dysfunction in a female patient characterized by hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or anorgasmy, or sexual pain disorders. (I) Can also be used for preventing or treating anxiety and panic disorders, social phobia, depression, psychoses, sleeping disorders, memory impairment, pulmonary hypertension, lung repair and lung development disorders, cancer including prostate cancer and pancreatic cancer, hepatic porphyria, gastrointestinal secretory disturbances, gastrointestinal disorders including colitis, Crohn's disease and inflammatory bowel disease, emesis, anorexia, pain, seasonal affective disorders, feeding disorders and pruritus (claimed).

Dwg.0/3

ACCESSION NUMBER: 2002-593206 [64] WPIDS
DOC. NO. CPI: C2002-167839
TITLE: New synthetic peptides active as **bombesin** receptor antagonists, useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or pruritis.
DERWENT CLASS: B05
INVENTOR(S): HIGGINBOTTOM, M; PRITCHARD, M C; STOCK, H T
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
GB 2369118	A	20020522	(200264)*		78
AU 2002017095	A	20020527	(200264)		
WO 2002040475	A1	20020523	(200264)	EN	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
EP 1334102 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
BR 2001015440 A 20040106 (200409)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
GB 2369118	A	GB 2000-28146	20001117
AU 2002017095	A	AU 2002-17095	20011116
WO 2002040475	A1	WO 2001-EP14402	20011116
EP 1334102	A1	EP 2001-996539	20011116
		WO 2001-EP14402	20011116
BR 2001015440	A	BR 2001-15440	20011116
		WO 2001-EP14402	20011116

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002017095	A	Based on	WO 2002040475
EP 1334102	A1	Based on	WO 2002040475
BR 2001015440	A	Based on	WO 2002040475

PRIORITY APPLN. INFO: GB 2000-28146 20001117

TI New synthetic peptides active as **bombesin** receptor antagonists, useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or. . .

AB GB 2369118 A UPAB: 20021007

NOVELTY - Synthetic peptides (I) are new.

DETAILED DESCRIPTION - Synthetic peptides of formula (I) and their salts (especially hydrochlorides, mesylates and sulfates) are new.

j = 0-2;
k = 0-1;
l = 0-3;
m = 0-1;
n = 0-2;
q = 0-1;
r = 0-1;

Ar = phenyl, pyridyl, pyrimidyl, thienyl, furyl, imidazolyl, pyrrolyl or thiazolyl, (all optionally substituted by 1-3 acetyl, alkoxy, alkyl, amino, CN, halo, OH, nitro, sulfonamido, sulfonyl, CF3, OCF3, CO2H, CH2CN, SO2CF3, CH2CO2H or (CH2)sNR7R8);

s = 0-3;

R7, R8 = H, 1-6C alkyl; or

NR7R8 = 5-7 membered aliphatic ring optionally containing 1-2 O atoms;

R1 = H, 1-6C alkyl or 5-7C cycloalkyl (optionally containing 1-2 N or O atoms);

R6 = H or Me; or

R1+R6 = C(O) or 3-7 membered aliphatic ring optionally containing an O or N atom;
Ar1 = Ar, indolyl or pyridyl-N-oxide;
R3-R5 = H or lower alkyl;
R2 = Ar, H, OH, alkoxy, -NMe2, -CONR9R10, or a group of formula (i)-(v);
R9, R10 = H or 1-6C alkyl; or
NR9R10 = 5-7 membered aliphatic ring optionally containing 1-2 O or N atoms;
p = 0-2;
Ar2 = phenyl or pyridyl;
X = a divalent radical derived from indane, tetrahydronaphthalene, naphthalene, benzimidazole, benzotriazole, 1,3-benzoxazole, benzothiophene, benzofuran, 1,3-benzothiazole, tetrahydroquinoline, tetrahydroisoquinoline, quinoline, isoquinoline or quinoxaline (all optionally substituted in the phenyl ring by R11 and R12), oxazole, pyridine, pyrimidine, pyrazine, pyridazine, 1,3,5-triazine, imidazole, 1,2,4-triazole, pyrrole, tetrazole, thiophene, 1,2,4-thiadiazole, imidazolidine, 1,3-thiazoline, furan, 1,2-oxazoline, 1,2-oxazolidine, 1,1-dioxo-1,2-thiazolidine, pyrazoline, pyrazole, 1,2,4-oxadiazoline, 1,2-thiazoline, pyrrolidine, 1,3,4-oxazole, 1,2,4-oxazole or benzene (all N atoms optionally substituted by lower alkyl);
R11, R12 = H, halo, OH, alkoxy, acetyl, nitro, CN, amino, CF3 or (CH2)tNR13R14;
t = 0-1;
R13, R14 = H, 1-6C alkyl or 5-7C cycloalkyl containing up to 2 O or N atoms;
provided that when r = 0, Ar is replaced by H.
INDEPENDENT CLAIMS are also included for the preparation of (I).
ACTIVITY - Vasotropic; Tranquilizer; Anxiolytic; Antidepressant; Antipsychotic; Sedative; Nootropic; Hypotensive; Cytostatic; Hepatotropic; Gastrointestinal; Antiulcer; Antiinflammatory; Antiemetic; Analgesic;Anabolic; Anorectic; Antipruritic.
Ovariectomized adult female Sprague Dawley rats (180-200 g) were housed in groups of 6 in a reversed lighting system of 12 hours light:dark. 2 weeks after ovariectomy they were used for sexual activity tests, They were tested using sexual stimuli: an intact sexually experienced male and a receptive female (ovariectomised, primed with 5 micro g estradiol benzoate dissolved in corn oil and injected subcutaneously 48 hours before the test and with 0.5 mg progesterone 4 hours before the test). Sexually naive test and control animals were used. (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-propionamide (Ia) (30-100 mg/kg) dose-dependently increased the difference in the % time spent investigating the male stimuli minus female stimuli, with a MED of 100 mg/kg. The effect of this dose was similar to that of progesterone.
MECHANISM OF ACTION - Bombesin (BB) receptor antagonists.
In BB1 and BB2 binding assays using CHO-K1 cells stably expressing cloned human decapeptide neuromedin B (NMB) (for BB1 assay) and gastrin releasing peptide GRP receptors (for BB2 assay), (S)-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-2-(4-(4-nitro-phenyl)-oxazol-2-ylamino)-propionamide (Ia) bound to NMB and GRP with Ki values of 4 and 24 nM, respectively.
USE - (I) Can be used for antagonizing the effects of neuromedin B and/or gastrin-releasing peptide at bombesin receptors, for treating sexual dysfunction which may be characterized by generalized unresponsiveness or age-related decline in sexual arousability in a male

or female patient, or treating sexual dysfunction in a female patient characterized by hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or anorgasmy, or sexual pain disorders. (I) Can also be used for preventing or treating anxiety and panic disorders, social phobia, depression, psychoses, sleeping disorders, memory impairment, pulmonary hypertension, lung repair and lung development disorders, cancer including prostate cancer and pancreatic cancer, hepatic porphyria, gastrointestinal secretory disturbances, gastrointestinal disorders including colitis, Crohn's disease and inflammatory bowel disease, emesis, anorexia, pain, seasonal affective disorders, feeding disorders and pruritus (claimed).
Dwg.0/3

TT TT: NEW SYNTHETIC ACTIVE **BOMBESIN** RECEPTOR ANTAGONIST USEFUL TREAT SEX DISORDER ANXIETY PAIN DEPRESS MEMORY IMPAIR HYPERTENSIVE CANCER COLITIS EMESIS FEED DISORDER.

L4 ANSWER 13 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-593205 [64] WPIDS
AB GB 2369117 A UPAB: 20021007
NOVELTY - Synthetic peptides active as **bombesin** receptor antagonists, useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or pruritis are claimed.
DETAILED DESCRIPTION - Synthetic peptides of formula (I) and their salts are new:
k = 0-2;
l = 0-3;
m = 0-1;
n = 0-2;
X = -CO-, -OCO, -SO- or -SO2-;
Ar = benzimidazolyl, benzofuryl, benzothiadiazolyl, benzothiazolyl, benzothienyl, benzopyrazinyl, benzotriazolyl, benzoxadiazolyl, furyl, imidazolyl, indanyl, indolyl, isoquinolyl, isoxazolyl, naphthyl, oxazolyl, phenyl, pyrazinyl, pyrazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, quinolyl, tetralinyl, tetrazolyl, thiazolyl, thienyl, or triazolyl each optionally substituted with 1-3 of amino, acetyl, 1-6C alkyl, alkoxy, cyano, halo, hydroxy, nitro, phenyl,pyridyl, pyrrolyl, isoxazolyl, phenoxy, tolyloxy, -CF3, -OCF3, -SO2CF3, -NHCONH2, -CO2H, -CH2CO2H, -CH2CN, SO2Me, SO2NH2, SO2Ph, -(CH2)qNR7R8, -CONR9R10, or CO2R11;
q = 0-2;
R7-R11 = 1-6C alkyl or cyclic alkyl of 5-7 atoms which may contain 1 or 2 O or N atoms; or
R7 + R8 or R9 + R10 = together with the N atom to which they are linked can form a 5-7-membered ring which may contain 1 or 2 O or N atoms;
Ar1 = Ar or pyridyl-N-oxide;
R1 = H or 1-6C alkyl or cyclic alkyl of 5-7 atoms which may contain 1 or 2 O or N atoms;
R2 = Ar or H, OH, alkoxy, -NMe2, -CONR12R13; or (II) - (VI)
p = 0-2;
Ar2 = phenyl or pyridyl;
R12, R13 = H, 1-6C alkyl or cyclic alkyl of 5-7 atoms;
R3-R5 = H or lower alkyl; and
R6 = H, methyl or forms with R1 a ring of 3-7C atoms which can contain an O or N atom, or
R1 + R6 = carbonyl.
INDEPENDENT CLAIMS are also included for:
(1) methods for the preparation of (I); and

(2) the intermediate (S)-2-amino-3-(1H-indol-3-yl)-N-(1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-2-methyl-propionamide (VIb).

ACTIVITY - Vasotropic; tranquilizer; anxiolytic; antidepressant; antipsychotic; somnogenic; nootropic; hypotensive; cytostatic; hepatotropic; antiinflammatory; antiemetic; analgesic; anorectic; antipruritic.

MECHANISM OF ACTION - **Bombesin** (BB) receptor antagonists.

BB1 and BB2 binding assays were carried out. CHO-K1 cells stably expressing cloned human decapeptide **neuromedin** B (NMB) (for BB1 assay) and **gastrin releasing peptide** **GRP** receptors (for BB2 assay) were routinely grown in Ham's F12 culture medium supplemented with 10% fetal calf serum and 2 mM glutamine. Cells were harvested by trypsinization, and stored frozen at -70 deg. C in Ham's F12 culture medium containing 5% DMSO until required. Binding studies to the BB receptors gave the following results: (IC50): BB1: 11 nM, BB2: 119 nM for 1H-indole-2-carboxylic acid ((S)-2-(1H-indol-3-yl)-1-((1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-carbamoyl)-1-methyl-ethyl)-amide.

USE - (I) can be used for antagonizing the effects of **neuromedin** B and/or **gastrin-releasing** **peptide** at **bombesin** receptors (claimed). They can be used for treating sexual dysfunction which may be characterized by generalized unresponsiveness or ageing-related decline in sexual arousability in a male or female patient, or treating sexual dysfunction in a female patient characterized by hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or **anorgasmy**, or sexual pain disorders (claimed). They can also be used for preventing or treating anxiety and panic disorders, social phobia, depression, psychoses, sleeping disorders, memory impairment, pulmonary hypertension, lung repair and lung development disorders, cancer including prostate cancer and pancreatic cancer, hepatic porphyria, gastrointestinal secretory disturbances, gastrointestinal disorders including colitis, Crohn's disease and inflammatory bowel disease, emesis, anorexia, pain, seasonal affective disorders, feeding disorders and pruritus (claimed).

Dwg.0/0

ACCESSION NUMBER: 2002-593205 [64] WPIDS
DOC. NO. CPI: C2002-167838
TITLE: New synthetic peptides, useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or pruritis are **bombesin** receptor antagonists.
DERWENT CLASS: B02 B03
INVENTOR(S): HIGGINBOTTON, M; PRITCHARD, M C; STOCK, H T; HIGGINBOTTOM, M
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO; (WARN) WARNER LAMBERT CO LLC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
GB 2369117	A	20020522	(200264)*		85
AU 2002016079	A	20020527	(200264)		
WO 2002040469	A1	20020523	(200264)	EN	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
EP 1334100 A1 20030813 (200355) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
BR 2001015414 A 20030909 (200369)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
GB 2369117	A	GB 2000-28104	20001117
AU 2002016079	A	AU 2002-16079	20011116
WO 2002040469	A1	WO 2001-EP14401	20011116
EP 1334100	A1	EP 2001-996536	20011116
		WO 2001-EP14401	20011116
BR 2001015414	A	BR 2001-15414	20011116
		WO 2001-EP14401	20011116

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002016079	A	Based on	WO 2002040469
EP 1334100	A1	Based on	WO 2002040469
BR 2001015414	A	Based on	WO 2002040469

PRIORITY APPLN. INFO: GB 2000-28104 20001117

TI . . . useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or pruritis are **bombesin** receptor antagonists.

AB GB 2369117 UPAB: 20021007

NOVELTY - Synthetic peptides active as **bombesin** receptor antagonists, useful for treating e.g. sexual disorders, anxiety, pain, depression, memory impairment, hypertension, cancer, colitis, emesis, feeding disorders or. . . Vasotropic; tranquilizer; anxiolytic; antidepressant; antipsychotic; somnogenic; nootropic; hypotensive; cytostatic; hepatotropic; antiinflammatory; antiemetic; analgesic; anorectic; antipruritic.

MECHANISM OF ACTION - **Bombesin** (BB) receptor antagonists.

BB1 and BB2 binding assays were carried out. CHO-K1 cells stably expressing cloned human decapeptide **neuromedin** B (NMB) (for BB1 assay) and **gastrin releasing peptide** **GRP** receptors (for BB2 assay) were routinely grown in Ham's F12 culture medium supplemented with 10% fetal calf serum and 2. . . nM, BB2: 119 nM for 1H-indole-2-carboxylic acid ((S)-2-(1H-indol-3-yl)-1-((1-(5-methoxy-pyridin-2-yl)-cyclohexylmethyl)-carbamoyl)-1-methyl-ethyl)-amide.

USE - (I) can be used for antagonizing the effects of **neuromedin** B and/or **gastrin-releasing** **peptide** at **bombesin** receptors (claimed). They can be used for treating sexual dysfunction which may be characterized by generalized unresponsiveness or ageing-related decline. . . or treating sexual dysfunction in a female patient characterized by hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders or **anorgasmy**, or sexual pain disorders (claimed). They can also be used for preventing or treating anxiety and panic disorders, social

phobia,. . .
TT TT: NEW SYNTHETIC USEFUL TREAT SEX DISORDER ANXIETY PAIN DEPRESS MEMORY IMPAIR HYPERTENSIVE CANCER COLITIS EMESIS FEED DISORDER **BOMBESIN** RECEPTOR ANTAGONIST.

L4 ANSWER 14 OF 15 PROMT COPYRIGHT 2004 Gale Group on STN

AB **ILLINOIS**
NYW005 11/18/1998 05:20 r f bc-IL-Minority-survey
(CHICAGO) Ranks of Minority Professors at Business Schools Set to Double as More Minorities Enter Business Ph.D. Programs, Survey Finds
CGW004 11/18/1998 07:00 r f bc-IL-Boise-Cascade
(ITASCA) Boise Cascade Office Products Names New Manager of Minority Business Development, Supplier Diversity
CGW009 11/18/1998 07:01 r f bc-IL-Arthur-Andersen
(CHICAGO) Arthur Andersen's KnowledgeSpace Delivers Powerful Business Tool
to Corporate Intranets
CGW013 11/18/1998 07:01 r f bc-IL-Mercury-Consultant
(CHICAGO) Mercury Finance Appoints Harshfield as Consultant
DEW003 11/18/1998 07:58 r f bc-IL-Horizon-Group
(CHICAGO) Major Changes At Horizon Group Properties Signify Beginnings of
a Success Story
CGW002A 11/18/1998 08:01 r v bc-IL-Ringling-Bros
(CLEVELAND) From the Soccer Field to the Center Ring, the Chicago Fire Defends Its Championship Title Against Cavorting Clowns and Soccer Playing
Pachyderms
CGW006 11/18/1998 08:01 r v bc-IL-American-Cancer-So
(SAN JOSE) Kids to Vote Against Smoking in Restaurants at Chicago's City Hall for Annual Great American Smokeout
MNW004 11/18/1998 08:02 r v bc-IL-Target-Speedway
(MOUNTAIN VIEW) Racecar Burns Rubber Downtown to Mark Target Stores' Title
Sponsorship of Inaugural Race at Chicago Motor Speedway
CGW023 11/18/1998 08:30 r f bc-IL-MedPartners
(HARVEY) How Healthcare Execs Can Benefit from the MedPartners Fallout
CGW012 11/18/1998 08:31 r v bc-IL-Loyola-Med-School
(MELVILLE) Cardinal George, WGN Radio Legend Wally Phillips to Join 1,400
Guests in Support of Loyola's Medical School Friday, Nov. 20
CGW001A 11/18/1998 09:01 r v bc-IL-Hoyt-Publishing
Hoyt Publishing Company Presents the P-O-P Show
THIS IS AN EXCERPT: COPYRIGHT 1998 PR Newswire Association, Inc.

ACCESSION NUMBER: 1998:604148 PROMT
TITLE: PRNewswire Midwest Summary Wednesday, November 18 to 4 P.M. EST.
SOURCE: PR Newswire, (18 Nov 1998) pp. 6183.
LANGUAGE: English
WORD COUNT: 3079
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX for New **Impotence** Diagnostic System
UroMetrics, Inc. Signs Worldwide Distribution Agreement for New **Impotence**
LAW011 11/18/1998 09:02 r f bc-OH-Full-Power-**Grp**.

L4 ANSWER 15 OF 15 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1993-19082 DRUGU T P S E
AB The methods of treatment of advanced prostate cancer, based on the agonistic analogs of LRF (LH-RH, luliberin) are reviewed. New therapeutic approaches utilizing antagonistic analogs of LRF are described.Analogs of LRF chemically linked to various cytotoxic radicals are also being developed. Combinations of LRF agonists or antagonists with superactive somatostatin analogues or with **bombesin/ gastrin releasing peptide** (**GRP**) antagonists are being investigated in order to delay or prevent the relapse and improve the therapy for prostate.
ABEX Treatment of male rats with Dunning R3327H prostate adenocarcinoma with D-Trp-6-LH-RH decreased tumor volume and reduced serum LH, FSH and testosterone. LH-RH analogs used for advanced prostate cancer include: triptorelin (D-Trp-6-LH-RH), buserelin, leuprolide and goserelin. Side-effects include **impotence**, loss of **libido** and hot flushes. Combinations of LH-RH agonists with antiandrogens e.g. flutamide, anandron (nilutamide) are also being used clinically. In patients with advanced 0prostate cancer, the combination of leuprolide with flutamide is superior to leuprolide alone. LH-RH agonists provide an effective palliative therapy resulting in objective stable disease or PR. A new approach to therapy of advanced prostate cancer is based on the development of cytotoxic LH-RH analogs with enhanced tumoricidal effects. Alkylating agents, platinum complexes, Adriamycin (doxorubicin) or anthraquinone derivatives can be linked to hormonal peptides like LH-RH agonists or antagonists. 3 Early antagonists including Ac D p Cl Phe 1,2,D Trp 3,D Arg 6,D Ala10 LH RH inhibited growth of the Dunning prostate tumor. Other antagonists discussed include cetrorelix (SB-75) which has been shown to produce a state of chemical castration. Somastatin analogs e.g. RC-160 (vapreotide) might inhibit prostate cancers by reducing the release of GH. A combination of RC-3095 (**bombesin**-receptor antagonist), (D-Trp6)-LH-RH (agonist) and RC-160 (somatostatin analog) decreased PC82 tumor growth in mice. (LJ)
ACCESSION NUMBER: 1993-19082 DRUGU T P S E
TITLE: Present Status of Agonistic and Antagonistic Analogs of LH-RH in the Treatment of Advanced Prostate Cancer.
AUTHOR: Schally A V; Comaru Schally A M; Gonzalea Barcena D
LOCATION: New Orleans, Louisiana, United States; Mexico, Mexico
SOURCE: Biomed.Pharmacother. (46, No. 10, 465-71, 1992) 38 Ref.
CODEN: BIPHEX ISSN: 0753-3322
AVAIL. OF DOC.: Department of Medicine, Tulane University School of Medicine, New Orleans, LA 70112, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB. . . to various cytotoxic radicals are also being developed. Combinations of LRF agonists or antagonists with superactive somatostatin analogues or with **bombesin/gastrin releasing peptide** (**GRP**) antagonists are being investigated in order to delay or prevent the relapse and improve the therapy for prostate.
ABEX. . . LH, FSH and testosterone. LH-RH analogs used for advanced prostate cancer include: triptorelin (D-Trp-6-LH-RH), buserelin, leuprolide and goserelin. Side-effects include **impotence**, loss of **libido** and hot flushes. Combinations of LH-RH agonists with antiandrogens e.g. flutamide, anandron (nilutamide) are also being used

clinically. In patients. . . castration. Somastatin analogs e.g. RC-160 (vapreotide) might inhibit prostate cancers by reducing the release of GH. A combination of RC-3095 (**bombesin**-receptor antagonist), (D-Trp6)-LH-RH (agonist) and RC-160 (somatostatin analog) decreased PC82 tumor growth in mice. (LJ)

CT. . . *OC; ADENOCARCINOMA *OC; *NIMAL-N; CASES *FT; RAT *FT; MOUSE *FT; IN-VIVO *FT; TOX. *FT; REVIEW *FT; CYTOSTATIC *FT; LULIBERIN-AGONIST *FT; **BOMBESIN**-ANTAGONIST *FT; LAB.ANIMAL *FT; RELEASING-FACTOR *FT

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